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ANNOUNCEMENT

RECOGNIZING the great advances in cardiovascular surgery and the increasing number of contributions by thoracic surgeons to this field, the Editorial Board and the membership of the American Association for Thoracic Surgery have with this issue officially changed the title of THE JOURNAL OF THORACIC SURGERY to THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY.

Contributions in the field of cardiovascular investigations and surgery will be acceptable only if they pertain to problems within the thorax. It is not intended that this JOURNAL publish papers dealing with the peripheral vascular system.

The Editorial Board

PULMONARY ARTERY WEDGE PRESSURE IN EXPERIMENTAL MITRAL INSUFFICIENCY

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Although a majority of authors[1, 2, 12, 14, 16, 24, 26] agree that, in the dog, the "mean pulmonary wedge pressure" is a faithful indication of the mean left atrial pressure, they are not of the same opinion concerning the transmission of these waves. We, therefore, have deemed it sufficiently important to investigate the transmission of the left atrial pressure to the pulmonary artery wedge pressure position in normal dogs, and in dogs with experimental mitral insufficiency and to determine, (1) whether the instantaneous changes of pressure in the left atrium are faithfully transmitted to the pulmonary artery wedge position; (2) to establish whether certain agents are capable of rendering the waves of mitral insufficiency more distinct, and (3) to study the influence of the increase of pulmonary vascular resistance on the transmission of the atrial wave of mitral insufficiency.

MATERIALS AND METHODS

Mongrel dogs weighing between 20 and 30 Kg. were prepared under intravenous Nembutal anesthesia. and intubated so that artificial respiration could be applied.

A cardiac catheter, of the type Goodale-Lubin No. 6 or No. 7, was introduced into an external jugular vein and advanced into a terminal branch of the right pulmonary artery, more frequently to the level of the inferior lobe and sometimes to the middle lobe level. It was generally wedged when the recording of the left atrial pressure began.

In some cases, a second catheter was introduced through the venous route into the pulmonary artery. In some experiments, the pulmonary artery wedge pressure was also recorded at the level of the left lower lobe.

Catheters were perfused at a slow rate (about 50 c.c. per hour) with normal saline solution containing 25 heparin units per cubic centimeter. The thorax was opened by an incision in the left fourth intercostal space. During

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the mediastinal dissection, care was taken to avoid injury of the pleura separating the two lungs. Mitral insufficiency was produced by the method of Chalnot and Benichoux,[4, 9] using a Dogliotti ring.

In experiments with an open thorax, respiration was checked except at the time of pressure recording. The left atrial pressure was measured by direct puncture with a long, fine needle connected to a No. 7 cardiac catheter

In experiments with a closed thorax, the animal was permitted to breathe normally. Left atrial pressure was measured in 2 cases by direct transthoracic puncture with a long, fine needle. This needle was introduced into the posterior part of the third left intercostal space and directed under fluoroscopic check toward the left atrium. In other cases, the pressure was recorded by left heart catheterization via the carotid artery using a No. 6 or No. 7 cardiac catheter.

Pressures were measured with the aid of two Sanborn electromanometers, and recorded by a Sanborn Twin-Viso electrocardiograph machine using a recording speed of 5 cm. per second.

The following agents were investigated in 9 dogs with an open thorax: (1) clamping of the aorta; (2) intravenous injection of 2 to 5 units of Pitressin*; (3) intravenous injection of 0.2 mg. of epinephrine; and (4) rapid injection of normal saline (100 c.c. in 5 seconds under 1.5 Kg. pressure) using the Dos Santos apparatus,[11] via a catheter in the inferior vena cava.

In 4 dogs which had been subjected to mitral insufficiency 8 to 22 days previously, a tracheal sound connected to an anesthesia apparatus and to a water manometer allowed us to create a pressure of 20 to 30 cm. of water in the bronchi and alveoli, thus producing a compression and an increase of the pulmonary capillary bed resistance.

During this insufflation, normal saline was rapidly injected via a catheter introduced into the inferior vena cava with the aid of Dos Santos apparatus.[11]

RESULTS

A. *Transmission of Normal Left Atrial Pressure Waves.—*

Our results in 11 dogs were as follows.

1. Except for certain deflections mostly "x" and "y," the positive waves were transmitted to the pulmonary artery wedge position with the same shape and also the same cyclic variations of amplitude (Fig. 1, Table I). The differences observed between the two positive wave tracings successively, and not simultaneously recorded, did not exceed those observed between several left auricular tracings recorded successively.

2. After opening the thorax, there was no modification of the right pulmonary artery wedge pressure, wave shape, or amplitude (Fig. 1, Table I).

3. Left pulmonary artery wedge pressure recorded on 2 dogs, after opening the thorax, revealed a damping of the wave as compared to the right pulmonary artery wedge pressure (Fig. 2).

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*Pitressin = Pitone Organon.

TABLE I. NORMAL PRESSURES IN THE DOG WITH OPEN AND CLOSED THORAX (MM. Hg)

DOG NO.	a			x			v			y			MEAN PRESSURE		
	P.A.W.			P.A.W.			P.A.W.			P.A.W.			P.A.W.		
	(C.T.)	(O.T.)	L.A.	(C.T.)	(O.T.)	L.A.	(C.T.)	(O.T.)	L.A.	(C.T.)	(O.T.)	L.A.	(C.T.)	(O.T.)	L.A.
1	6.5	7.5	7	3.5	4	3	6.5	7.5	7	3.5	3	1.5	5.5	5	4
2	11	12	11	5.5	6	4.5	10	9	8.5	6.5	6	1.5	7	6.5	5
3	11	10.5	10	1.5	1.5	−2	6	5	4	3.5	2	1	5	4.5	4
4	9.5	11.5	11.5	1	2	−3	7	6.5	7	1.5	2	−2	4.5	4.5	4
5	5.5	5.5	5	3.5	3	2.5	8	7	5	3	3	2	5	4	3
6	7.5	7.5	7	3	2	1.5	7	6.5	6	4	2	3	4.5	3	3.5
7	10	8	7.5	−4	−4	−3	12.5	12.5	9	1	0	−1.5	5.5	5	3.5
8	7	7.5	6.5	2	2	1.5	5.5	6	6	4	4	4.5	3	3.5	3
9	6	8	8.5	0	0	1	8	9	9.5	0	0	1	2.5	2	2.5
10	5	5.5	6	2	2.5	2	4.5	4	4	2.5	2.5	1.5	3.5	3.5	3
11	7	6.5	7	4	3	3.5	7	6.5	5	4.5	4	4	6	5.5	4.5

L.A.—left atrial pressure; P.A.W.—pulmonary artery wedge pressure; O.T.—open thorax; C.T.—closed thorax.

TABLE II A. PRESSURES IN THE DOG WITH OPENED THORAX AFTER EXPERIMENTAL MITRAL INSUFFICIENCY (MM. Hg)

DOG NO.	a		x		v		y		MEAN PRESSURE	
	R.P.A.W.	L.A.	R.P.A.W.	L.A.	R.P.A.W.	L.A.	R.P.A.W.	L.A.	R.P.A.W.	L.A.
2	13.5	15	7	7	14	15.5	7	7	10	11
3	24	23.5	8	8	23.5	24.5	19	19	16.5	15.5
4	11	8.5	6.5	6	17	18	5.5	1.5	11.5	11
5	10.5	9	2	2	12.5	12	7.5	7	8	6.5
7	22	30	10	10	56	60	10	−16	30	28
8	5.5	7	4	5	12.5	14	4	0	8	7
9	13.5	15	4	5	13	15	5.5	0	7.5	7
10	8.5	8	4.5	4	11.5	13	5	2	8	7
11	–	–	18	20	56	52	19	−8	28	26.5

TABLE II B

DOG NO.	a		x		v		y		MEAN PRESSURE	
	R.P.A.W.	L.P.A.W.	R.P.A.W.	L.P.A.W.	R.P.A.W.	L.P.A.W.	R.P.A.W.	L.P.A.W.	R.P.A.W.	L.P.A.W.
4	11	9	6.5	7.5	17	12.5	5.5	6	11.5	10.5
8	5.5	5.5	4	4.5	12.5	8	4	5	7.5	7

R.P.A.W.—right pulmonary artery wedge pressure; L.A.—left atrial pressure; L.P.A.W.—left pulmonary artery wedge pressure.

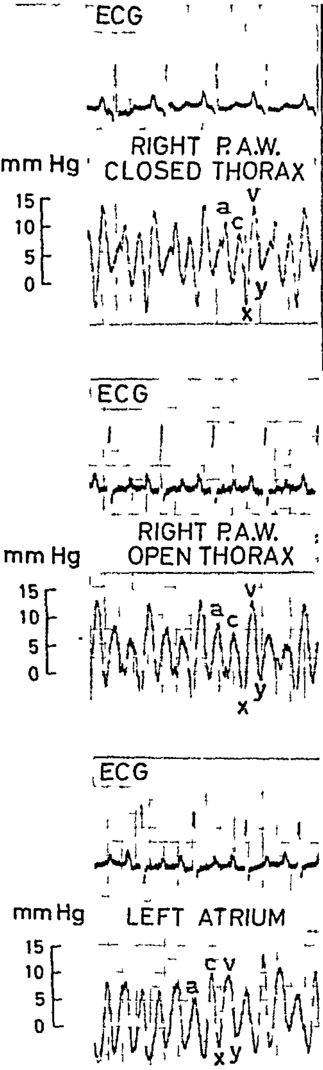


Fig 1

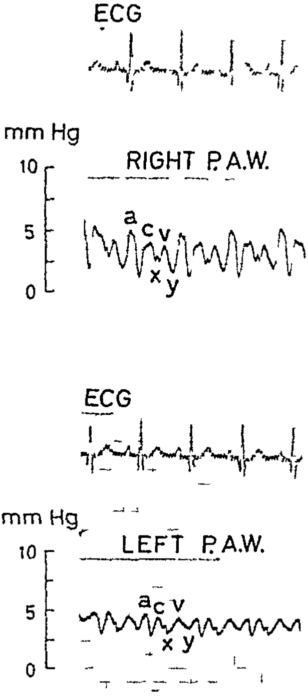


Fig 2

Fig 1—(Dog 7) Right P A W—right pulmonary artery wedge On the left atrial tracing, three waves *a*" *c*' and '*v*' can be seen They are transmitted to the right pulmonary artery wedge position with equal amplitude The right pulmonary artery wedge tracing with open and closed thorax is the same

Fig 2—(Dog 10) Right P A W—right pulmonary artery wedge Left P A W—left pulmonary artery wedge The pulmonary artery wedge tracing recorded on the side of the thoracotomy (left side) enables us to recognize the three atrial waves but they are less ample than on the opposite side

B. *Transmission of the Left Atrial Pressure Wave in Mitral Insufficiency.*—

1. *Experiments in 9 dogs with an open thorax:*

   a. In 7 dogs, a typical mitral insufficiency wave was recorded in atrial tracings. This wave was found on the right pulmonary artery wedge pressure tracing. It was also identical both in form and amplitude with the atrial wave (Fig. 3, Table II A).

   b. In 2 dogs showing a definite moderate mitral insufficiency verified by finger palpation and at autopsy, the right pulmonary artery wedge tracing did not show a typical regurgitation "v" wave. The left atrial curve, furthermore, did not reveal a characteristic mitral insufficiency wave and its shape was the same as that of the pulmonary artery wedge tracing.

   c. In 2 dogs, we recorded the pulmonary artery wedge pressure in both lungs (Table II B). The left mean pulmonary artery wedge pressure was the same as in the right lung, but the cyclic variations of the left lung reading were "damped." The left wave was still visible although less apparent and of lesser amplitude. Its peak was retarded as compared with the right pulmonary artery wedge pressure tracing by a time interval of 0.05 to 0.06 second.

2. *Dogs with a closed thorax:* Twelve dogs underwent an experimental mitral insufficiency. Six of these dogs developed a severe mitral insufficiency and died of acute pulmonary edema within a week. A 1 to 3 week follow-up study of the remaining operated dogs showed the following results.

   a. The regurgitation "v" wave on the left atrial tracing was seen also on the right pulmonary artery wedge pressure curve and was of about the same amplitude (Fig. 4, Table III A).

   b. In spite of the resorption of the pneumothorax and the absence of liquid in the left pleura on 2 of the dogs examined 15 days and 3 weeks postoperatively, a damping of the left pulmonary artery

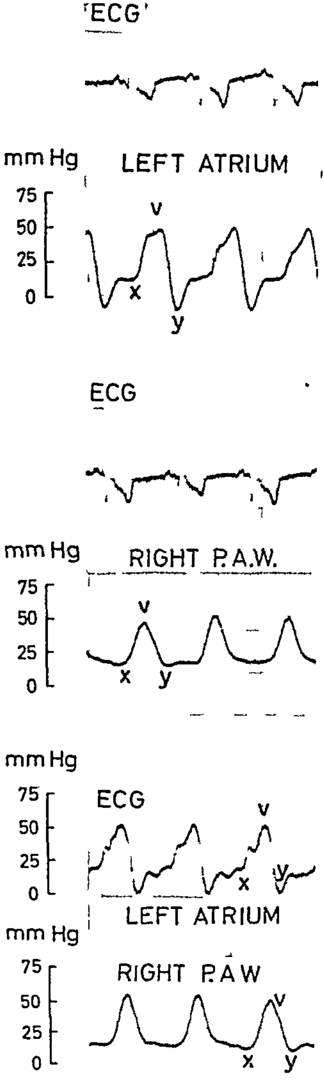
TABLE III A. PRESSURES IN THE DOG WITH CLOSED THORAX AFTER EXPERIMENTAL MITRAL INSUFFICIENCY (MM. Hg)

DOG NO.	a		x		v		y		MEAN PRESSURE	
	R.P.A.W.	L.A.	R.P.A.W.	L.A.	R.P.A.W.	L.A.	R.P.A.W.	L.A.	R.P.A.W.	L.A.
1	10	10	5	4	10	10.5	6.5	3	6.5	5
2	6	5	5	4	15	16	6	3	7.5	6
3	7	7.5	5	4	17	15	5	3	7	6
4	5.5	4	2.5	1.5	8	7.5	2.5	1	5	3.5
5	8.5	9	-1	-1	11.5	11.5	3	0	5	4
6	13	13	6	5	11.5	12	5	3	7.5	7

TABLE III B

DOG NO.	a		x		v		y		MEAN PRESSURE	
	R.P.A.W.	L.P.A.W.	R.P.A.W.	L.P.A.W.	R.P.A.W.	L.P.A.W.	R.P.A.W.	L.A.	R.P.A.W.	L.P.A.W.
3	7	6	5	5.5	17	10	5	6	7	6.5
4	5.5	5	2.5	4	8	5.5	2.5	4.5	5	5

R.P.A.W.—right pulmonary artery wedge pressure; L.A.—left atrial pressure; L.R.A.W.—left pulmonary artery wedge pressure.



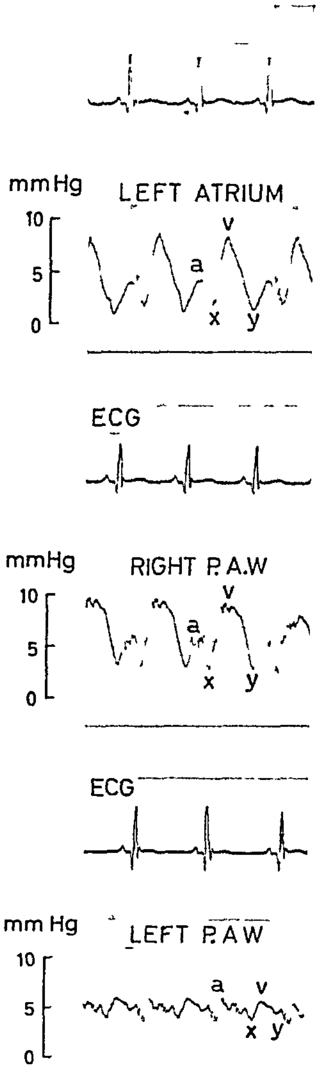


Fig 3

Fig 4

Fig 3 —(Dog 11) Right P.A.W.—right pulmonary artery wedge On the left atrial tracing there is a typical v wave of mitral regurgitation This wave is transmitted to the right pulmonary artery wedge position with the same amplitude The difference between the two tracings is due to an absence of transmission of the left atrial y wave below the x' wave

Fig 4 —(Dog 4) Right P.A.W.—right pulmonary artery wedge Left P.A.W.—left pulmonary artery wedge The left atrial v wave of mitral insufficiency is transmitted to the right pulmonary artery wedge position with the same amplitude On the left side there is an important damping of the atrial waves mainly the v wave the apex of which is delayed with respect to that of the tracing recorded on the right side The mean pressures of the left and right pulmonary artery wedge positions are identical and slightly greater than that of the left atrium

TABLE IV

Influence of the Clamping of the Aorta (mm. Hg)

DOG NO.	a				x				v				y				MEAN PRESSURE			
	BEFORE		DURING		BEFORE		DURING		BEFORE		DURING		BEFORE		DURING		BEFORE		DURING	
	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.
1	18	16.5	23	22	8	8	20	18	34	33	62	61	10	2	20	8	25	23	43	40.5
2	20	21	25	25.5	11	8	22	21	30	28.5	54	56	11	7	21	0	14	12	29.5	26.6
3	24	23.5	33	38.5	18	18	30	33	23.5	23.5	57	57	3	1	27	13	16.5	15.5	34	31
4	26	20	25.5	23	21	17	30	29.5	46	46	71	71	23	0	30	4	39	37	49	46
5	38	34	43	42	29	30	37	35	57	58	107	109	31	21	36	25	40	36	68	64

Influence of Intravenous Injection of Pitressin (mm. Hg)

DOG NO.	DOSAGE	a				x				v				y				MEAN PRESSURE			
		BEFORE		AFTER		BEFORE		AFTER		BEFORE		AFTER		BEFORE		AFTER		BEFORE		AFTER	
		R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.
1	2U	14	12.5	21	23	6	6	12	10	21	22	48	47	7.5	0	12	3	14	13	37	35
2	2U	13.5	15	20	21	7	7	11	8	14	15.5	30	28.5	7	7	11	7	10	11	21	21
3	4U	24	23.5	41	43	18	18	34	32	23.5	23.5	89	86	19	19	34	0	16.5	15.5	58	56
4	4U	11	8.5	39	41	6.5	6	32	34	17	18	83	85	5.5	1.5	25	0	11.5	11	68	65
5	5U	10.5	9	38	34	2	2	29	30	12.5	12	57	58	7.5	7	31	21	7	6.3	40	36
8	4U	5.5	7	21	19	4.5	5	16.5	10	12.5	14	125	125	4.5	1	14.5	0	8.5	7	72	68

Influence of Intravenous Injection of 0.2 mg. of Epinephrine (mm. Hg)

DOG NO.	a				x				v				y				MEAN PRESSURE			
	BEFORE		AFTER		BEFORE		AFTER		BEFORE		AFTER		BEFORE		AFTER		BEFORE		AFTER	
	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.
7	–	–	–	–	–	–	–	–	72	80	126	121	22	25	25	25	48	52	78	75
9	13.5	15	19	20	4	5	6	7	13	15	27	26	5.5	0	9	2	7.5	7	14	13
10	8.5	8	13	12	4.5	4	7	5	11.5	13	29	27.5	5	2	9	7	8	7	17	14

Influence of the Rapid Injection of 100 c.c. of Normal Saline (mm. Hg)

DOG NO.	a				x				v				y				AFTER THE INJECTION			
	BEFORE		DURING		BEFORE		DURING		BEFORE		DURING		BEFORE		DURING		v		y	
	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.	R.P. A.W.	L.A.
5 (B)	8.5	8	13	12	4.5	4	7	6.5	6	5	14	12	3.5	3	7	5	9.5	8.5	5.5	4
8 (B)	–	–	–	–	–	–	–	–	35.5	36	62	57	8.5	7	15	12	34	35	10	9
9	13.5	15	19	20	4	5	6	7	13	15	29.5	31	5.5	0	8	3	16	15.5	6.5	1
10	–	–	–	–	–	–	–	–	11.5	13	23	24	5	2	9	6	14	14.5	6.5	4

R.P.A.W.—right pulmonary artery wedge; L.A.—left atrium.

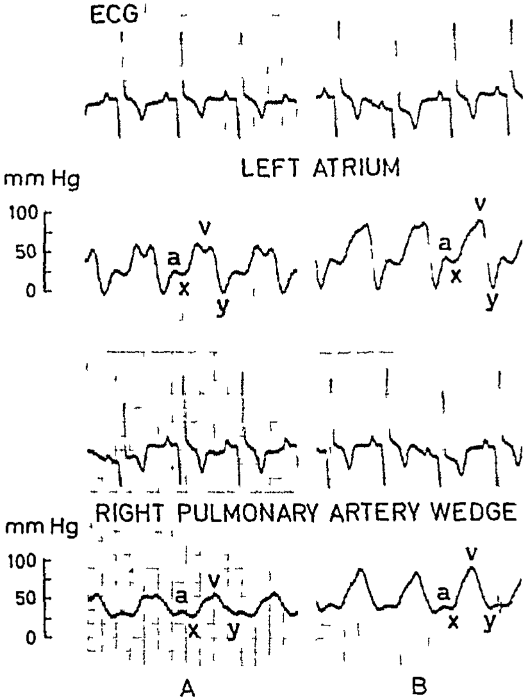


Fig 5.—Influence of aortic clamping *A*, Before, *B* after The increase of pressure of the regurgitation 'v' wave is equal in the two positions

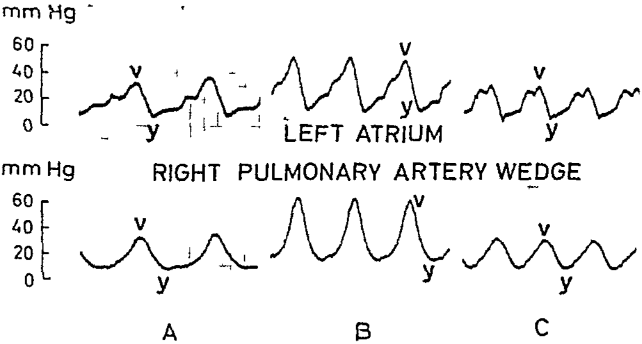


Fig 6.—The influence of a rapid intravenous injection of 100 c c of physiologic liquid *A*, Before *B*, Immediately after *C*, 3 minutes after

wedge pressure, involving principally the regurgitation "v" wave, was found (Fig. 4, Table III B). The mean pressure was exactly the same as the pressure recorded for the right lung.

C. *Action of Various Agents on the Pressure Curves of the Left Atrium and the Pulmonary Artery Wedge Pressure in Experimental Mitral Insufficiency* (see Table IV and Figs. 5 and 6).—

1. For the first three agents (clamping of the aorta, intravenous injection of 2 to 5 units of Pitressin, intravenous injection of 0.2 mg. of epinephrine) the following results were noted.

a. The increase of the mean left atrial pressure observed was transmitted to the pulmonary artery wedge, the pressure in the latter being mostly a few millimeters of mercury greater than the left atrial pressure (Table IV).

b. These agents produced an increase of the atrial regurgitation "v" wave *that was much more important than that of the "a" wave* (Table IV, Fig. 5).

c. The pulmonary artery wedge tracing faithfully followed the modifications observed at the positive waves, mainly at the "v" wave regurgitation. Whereas, on the initial tracing, the negative "x" wave was generally well transmitted, the pulmonary artery wedge "y" wave often did not go below the "x" level (Table IV, Fig. 5).

2. The rapid injection of normal saline solution produced a definite and transitory increase of the "v" wave, more apparent than for the "a" wave, the corresponding pressures at "x" and "y" being *only slightly increased* (Table IV, Fig. 6).

D. *Influence of the Increase of Pulmonary Vascular Resistance on the Transmission of the Left Atrial Waves.*—

1. During the insufflation of the lungs under pressure, a damping of the left atrial and pulmonary artery wedge tracings was observed (Fig. 7, *A* and *B*).

2. One also noticed a damping of the pulmonary artery wedge "v" wave as compared to the wave recorded in the left atrium.

3. The transmission time of the atrial "v" wave (measured from the apex of the wave) to the pulmonary artery wedge position was increased (Fig. 7, *A* and *B*).

4. The rapid injection of normal saline solution intravenously during the insufflation of the lung under pressure caused, on the one hand, an increase of the "v" waves which was *more apparent* on the pulmonary artery wedge tracing and, on the other hand, a shortening of the transmission delay of the left atrial "v" wave (Fig. 7, *C*).

5. Immediately after the end of insufflation of the lungs, a transitory increase of the "v" wave was observed both on the pulmonary artery wedge tracing and on the left atrial tracing (Fig. 7, *D*).

6. With respect to the pulmonary artery tracing, during the insufflation, a damping of the pulmonary artery wedge "v" wave was observed, as well as a

delay in the recording of its apex with respect to the apex of the pulmonary arterial systolic wave.

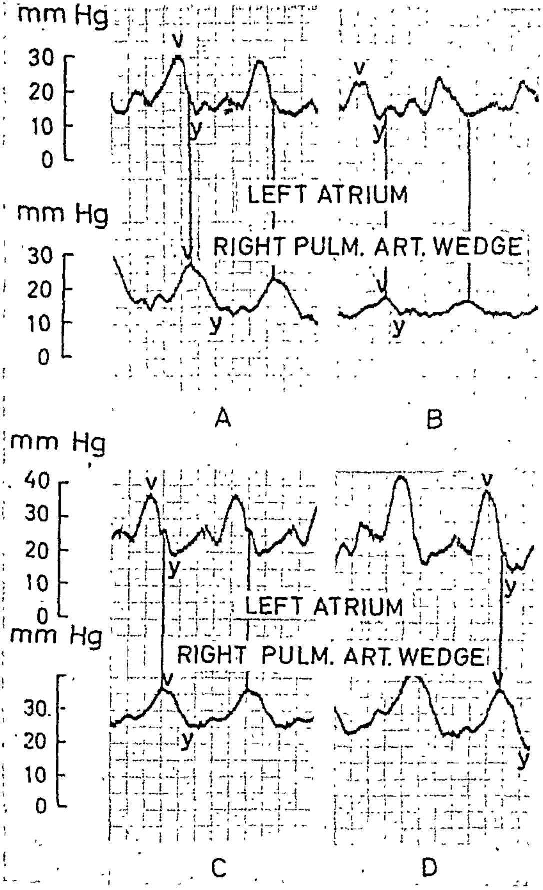


Fig. 7.—Influence of rapid intravenous injection of 100 c.c. of normal saline during the lung insufflation.

A, Before the lung insufflation.

B, During the insufflation under a pressure of 30 cm. water.

C, Immediately after the rapid intravenous injection of 100 c.c. of normal saline during the lung insufflation.

D, Immediately after the lung insufflation.

On the *B* tracing, a damping and a supplementary transmission delay of the apex of the P.A.W. "v" wave is observed, with respect to that of the left atrium. The rapid injection of normal saline almost restores the P.A.W. "v" wave to its initial amplitude and suppresses the supplementary delay of transmission of the left atrial "v" wave to the P.A.W. position.

COMMENTS

A. *Transmission of the Normal Left Atrial Pressure.*—

In our experiments, the thorax was opened by a left intercostal incision. The catheter tip was at the right lung level. The thin pleura separating the two lungs was left untouched and therefore a right-sided pneumothorax was avoided.

This condition must be fulfilled in order to have a good transmission of the left atrial waves toward the pulmonary artery wedge position. In two "open-thorax" experiments, the pulmonary artery wedge pressure in both lungs was recorded, and there was decisive evidence of damping on the pressure curve of the left lung as compared with that of the right lung.

B. *Transmission of the Atrial Pressure Curve in Mitral Insufficiency.*—

In the case of "open-thorax" dogs having undergone a mitral insufficiency by a left thoracotomy approach, under our own experimental conditions, a good transmission of the atrial waves and, mainly, of the regurgitation "v" wave to the right pulmonary artery wedge position was observed. In some dogs, which in spite of proved mitral insufficiency, there was no typical "v" wave on the right pulmonary artery wedge position, the "v" wave was also absent in the left atrial curve.

In similar human cases where moderately severe mitral insufficiency was verified by palpation, regurgitation "v" waves were not discernible on left atrial curves. These human cases have been reported by Wynn and his collaborators,[28] Venner and Holling[25] and, also, by Ankeney and his colleagues.[3]

As regards the dog, the effect of a left pneumothorax on left atrial wave transmissions can be seen. On the right side, where there was no pneumothorax, all atrial waves were correctly transmitted. On the left side, a damping effect could be seen when the recording was made in the pulmonary artery wedge position. A midline incision of the thorax, as practiced by Ankeney and his co-workers,[2] or a rupture of the pleura separating the lungs during a left-sided surgical approach, can be the cause of poor transmission of regurgitation "v" waves.

In "closed-thorax" dogs, our findings were similar to those of Haddy and his co-workers[14] who found a good transmission of regurgitation waves 2 weeks later in operated dogs. In this particular case, the wave amplitude was of 40 mm. Hg.

For even lower pressures, we have experienced good wave transmission in our results. Coelho and associates[10] were not able to put into evidence any typical pulmonary artery wedge pressure on "closed-thorax" dogs when the mitral valves were experimentally rendered insufficient.

Even without any liquid reaction of the pleura, the effect of a left pneumothorax on the transmission of atrial waves continued, even when the pneumothorax was completely resorbed. In fact, 15 days to 3 weeks after operation, a damping of the pulmonary artery wedge pressure curve at the level of the inferior left lobe has still been observed in 2 dogs.

C. *Action of Various Agents on the Pressure Curves of the Left Atrium and the Pulmonary Artery Wedge Pressure in Experimental Mitral Insufficiency.*—

In the dog with the "closed-thorax," Vuylsteek[26] noted that the increase of mean left atrial pressure produced by the obliteration of the aorta or the injection of epinephrine or Pitressin, was transmitted to the pulmonary artery wedge position. Our experiments confirmed Vuylsteek's findings on the dog with the open thorax and also showed that the increase of the left atrial "a" and "v" waves are found practically to be equal on the pulmonary artery wedge tracings.

These three agents, as well as the rapid intravenous injection of normal saline solution produced an increase of the regurgitation "v" wave which was more important than that of the wave "a", it was only temporary in the case of injection of normal saline solution.

After the latter test, left atrial and pulmonary artery wedge diastolic pressures usually did not return to the initial level. Ankeney,[1, 2] and Henry[1] and Ferguson[13] and their associates observed the same increase of the left atrial diastolic pressure after injection of liquid of approximately the same volume as that used in our own experiment. This might also be caused by the increase of the blood volume.

D. *Influence of the Increase of Pulmonary Vascular Resistance on the Transmission of the Left Atrial Waves in Experimental Mitral Insufficiency.*—

1. The increase of pulmonary vascular resistances in human mitral disease is a well known phenomenon. On the contrary, in the dog subjected to a mitral stenosis, Haddy and collaborators[14] proved that after 10 months there was no increase of these resistances. Owing to the fact that the time required for the setting of these increased resistances in the dog is certainly longer than 10 months, we preferred to use a simple and rapid technique which consists of insufflation of the lungs of the experimental animal under pressure. Its mechanism is certainly not the same as in human mitral disease but the place where the increase of the resistance acts is of little importance for our study. The decrease of the pulmonary vascular network caliber produced by insufflation under pressure is without doubt, if one refers to the fine angiopneumographies of Rimini.[20]

2. Our observations confirm the damping of the pulmonary artery wedge tracing observed in man by Shaffer and Silber[21] in the case of mitral disease with increase of pulmonary arteriolar resistances, as well as by Bjork,[6] Lee,[19] during Valsalva's test, and Werko[27] and their collaborators during positive respiration.

3. The delay in the transmission of the left atrial regurgitation wave observed by comparing the pulmonary artery wedge "v" wave to the left atrial "v" wave or to the pulmonary artery tracing showed a shortcoming during the determination of mitral insufficiency in man on a pulmonary artery wedge tracing.

It should be noted that this transmission delay, associated with a damping of the ''v'' wave, may result in the lowering of the apex of the pulmonary artery wedge "v" wave after the closing wave of the pulmonary artery. Its precession in respect of the latter was admitted by Lagerlöf and Werkö,[18] and Soulie and co-workers[22] as being a criterion of mitral insufficiency.

More recently, some authors, among whom Soulie[23] and Blum[7] and their associates have considered this criterion (precession of the pulmonary artery wedge "v" wave in respect to the closing wave of pulmonary artery) as being unreliable. Soulie admits, however, that in the presence of regular sinus rhythm, and in determined conditions, it may be a useful adjuvant in diagnosis. Soulie and collaborators[23] have also argued that the "pulmonary artery wedge" tracing could, in the case of mitral insufficiency, have a different morphology depending on the territory where it is recorded and on the tension applied to the extremity of the catheter.

The modifications observed by these authors may be explained in the following manner: (1) the variable anatomic alterations in one or another place of the lung also suggest various vascular resistances, (2) the relations between the vascular walls and the catheter orifice with an exaggerated tension may obliterate, at least partly, the catheter orifice (these two factors are an obstacle to the transmission on the regurgitation wave and may offset its apex with respect to the pulmonary artery closing wave), and (3) the rapid injection of normal saline solution, creating a sudden distention of the pulmonary vascular bed, practically restores the regurgitation wave "v" to its initial amplitude and suppresses the additional delay of the transmission of the left atrial "v" wave created by the insufflation of the lungs.

However, we cannot consider this technique as being free from danger as far as man is concerned. Yet it is possible that immediately after a Valsalva test, which creates a sudden and transitory flow into the lungs, the recording of the pulmonary artery wedge curve brings about modifications similar to those observed during the rapid injection of normal saline solution. Providing the cardiac output can be sufficiently increased, an effort test could achieve the same result.

CONCLUSIONS

1. In normal dogs having undergone a left thoracotomy, there was a good transmission of the positive left atrial waves toward the right pulmonary artery position. The left position tracing was damped. The opening of the thorax modified neither the form nor the amplitude of the right pulmonary artery wedge pressure tracing.

2. In the dog submitted to an experimental mitral insufficiency by a left thoracotomy approach, the left atrial regurgitation wave was correctly transmitted toward the right pulmonary artery wedge position. In dogs in which no regurgitation wave was discernible on the right pulmonary artery wedge position tracing, the wave was also absent on the left atrial recording. A

pneumothorax gave rise to a damping of the left pulmonary artery wedge pressure curve as compared to the right and a retardation of the peak of the regurgitation wave.

3. In "closed thorax" dogs having undergone a mitral insufficiency and breathing normally, examined 1 to 3 weeks after, a good transmission of the left atrial regurgitation wave toward the right pulmonary artery wedge position was found as experienced in "open thorax" dogs under artificial respiration. A damping of the left pulmonary artery wedge pressure tracing still occurred, in spite of total pulmonary re-expansion and absence of liquid in the pleural cavity.

4. Influence of mechanical or pharmacodynamic agents. (a) In dogs subjected to mitral insufficiency, the obliteration of the aorta and intravenous injection of Pitressin or epinephrine produced an increase of the mean left atrial pressure as well as the amplitude of the regurgitation wave. (b) These modifications were faithfully transmitted to the right pulmonary artery wedge position. (c) A rapid intravenous injection of normal saline determined a definite but transitory increase of the regurgitation wave in equal proportions both on the left atrial tracing and on the pulmonary artery wedge tracing.

5. Influence of the increase of pulmonary vascular resistance. (a) The increase of pulmonary vascular resistances created by the insufflation of the lungs under pressure produced a damping and an additional delay in the transmission of the mitral insufficiency wave to the pulmonary artery wedge position. (b) During the insufflation of the lungs under pressure, the rapid intravenous injection of normal saline restored the pulmonary artery wedge regurgitation wave practically to its initial amplitude and cancelled the additional delay in the transmission to the pulmonary artery wedge position.

SUMMARY

In dogs with open and closed thoraces, there was a good transmission of the mean left atrial pressure to the pulmonary artery wedge position.

The normal and pathologic (mitral insufficiency) positive waves were faithfully transmitted only to the side opposite the thoracotomy. On the operated side, there was a damping of the pulmonary artery wedge tracing which persisted for at least 3 weeks after the thoracotomy.

The mitral regurgitation wave could be considerably increased under the influence of various mechanical or pharmacodynamic agents. These modifications were faithfully transmitted to the pulmonary artery wedge position. The increase of pulmonary vascular resistance created a damping and a delay in the transmission of the mitral regurgitation wave on the pulmonary artery wedge tracing. These modifications temporarily disappeared through a rapid intravenous injection test of normal saline solution.

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PROLONGED VENTRICULAR FIBRILLATION

An Experimental Study in the Closed Chest Animal Utilizing a Pump-Oxygenator

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INTRODUCTION

PRIOR to the development of the pump oxygenator and realization of circulatory substitution, ventricular fibrillation was well known as a fatal and irreversible arrhythmia Without support of the coronary and cerebral circulation, experience proved that the fibrillating heart, after several minutes, could seldom be restored to a satisfactory rhythm either by chemical or electrical means[1,2] Since the advent of intracardiac surgery, evidence is accumulating that ventricular fibrillation is a relatively innocuous arrhythmia when it occurs during pump oxygenator support[3]

Our interest in the deliberate use of ventricular fibrillation in the intact animal resulted from a search for a satisfactory method of producing cardiogenic shock This arrhythmia appeared to satisfy the criteria of an experimental state which was reversible, easily induced, and during which the animal was totally dependent upon extracorporeal support

Our purpose is to report satisfactory prolonged substitution for the fibrillating canine heart with the bubble oxygenator These experiments were done with peripheral cannulation of the femoral vessels in the normothermic closed chest animal Successful electrical defibrillation of the heart following 2 to 3 hours of deliberate fibrillation, is in accord with Wiggers' early demonstration that a well oxygenated myocardium is the vital requirement for restoration of sinus rhythm[4]

METHODS

Ten healthy mongrel dogs varying in weight from 12 to 34 Kg were anesthetized with intravenous sodium pentobarbital, intubated, and mechanically respirated

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Connection to the oxygenator was accomplished by peripheral cannulation. The largest catheter possible (usually 20 Fr.) was introduced through the left femoral vein into the inferior vena cava to the level of the diaphragm. For arterial input the right femoral artery was cannulated in a retrograde manner.

Systemic arterial pressure was measured by catheterization of the left femoral artery and connection to a Statham P23D pressure transducer. Recordings were made on a Sanborn Twin-Viso and monitored on the Viso-Scope. Central venous pressure was measured with a water manometer by cannulation of the right jugular vein. The electrocardiogram (Lead II) was recorded on a Sanborn Cardiette and monitored as necessary on the Viso-Scope. The animal was given intravenous heparin, 1 mg. per kilogram. The blood in the oxygenator system was heparinized at 3 mg. per 100 ml. Animal temperature and temperature of the blood in the debubbling chamber were measured with thermistor probes and a Yellow Springs telethermometer.

Ventricular fibrillation was induced using external chest electrodes. The Morris apparatus, capable of voltage up to 220 and impulse duration of 0.5, 1.0 sec., has been used. Evidence of ventricular fibrillation was noted by absence of the apical impulse, the characteristic fibrillatory pattern on the electrocardiogram and the immediate drop of arterial pressure to a static level of 5 to 10 mm. Hg. Following the onset of fibrillation, extracardiac substitution was begun, usually within 10 to 30 seconds. Venous pH was drawn at 15-minute intervals. Serum potassium was determined prior to defibrillation in occasional experiments.

After varying periods of fibrillation, the heart was defibrillated through the intact chest, using large external electrodes 8.5 cm. in diameter. For this purpose the Electrodyne defibrillator,* capable of 750 volts at 0.15 sec., has been successful.

RESULTS AND OBSERVATIONS

Technique of Fibrillation and Defibrillation.—The electrical factors necessary for the induction of ventricular fibrillation in the intact animal were established largely by trial. It may be seen from Table I that there is a rough correlation of animal weight to fibrillation voltage. Dogs, from 10 to 20 Kg., usually required 110 to 135 volts. The larger dogs, from 20 to 30 Kg., required 135 to 160 volts at 0.5 sec. duration. An impulse duration of less than 0.5 sec. was not reliable for fibrillation and a shock of 1.0 sec. was no more effective than 0.5 sec. Although body weight altered fibrillation voltage and time requirement, equally important in the intact animal was the amount of muscle and fat on the chest wall and the position and contact of the external electrodes. On the exposed canine heart, Mackay and associates[5] found that currents of low value and long duration were necessary to produce fibrillation. Early work by Hooker, Kouwenhoven, and Langworthy[6] demonstrated the ease with which ventricular fibrillation may be established in the canine heart by relatively low currents. They found that one milliampere of current, applied directly to the ventricular musculature, was sufficient to cause fibrillation, and the extreme apex was as sensitive as any other point in the ventricles.

For successful defibrillation in the intact animal, due to the spread of current *over the tissues on either side of the thorax, the countershock must be increased* three to four times the value required for fibrillation. Kouwenhoven and co-workers[7] state that 4 or 5 amperes is necessary, while Guyton and

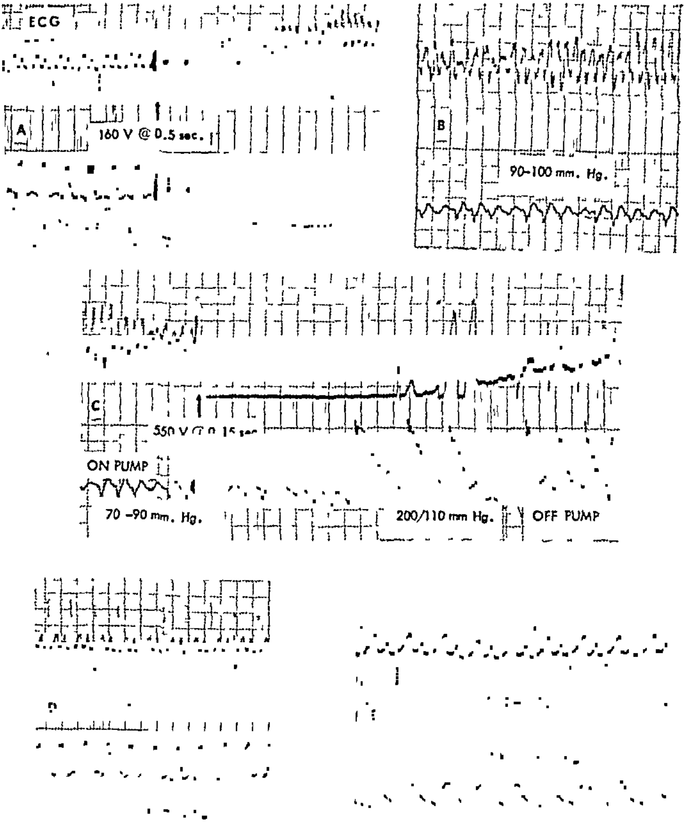

Fig 1.—Experiment 13. 19.8 Kg. dog. *A*, Introduction of ventricular fibrillation in closed chest animal.

B, After 2 hours of ventricular fibrillation, electrocardiogram shows fine wave with good amplitude. Mean arterial pressure of 90 mm. Hg with perfusion of 65 to 70 ml./Kg.

C, Defibrillation after 2½ hours of total body perfusion. Prompt resumption of sinus rhythm and exaggerated systemic arterial pressure with hypervolemia.

D, Prefibrillatory electrocardiogram and arterial pressure pattern (compare to *A*) 1 to 5 minutes after defibrillation.

E, Initial hypervolemia restored to normovolemia.

Satterfield[8] believe approximately 20 amperes to be satisfactory. They found, as have other investigators, that the important factor in defibrillation is the density of current flow through the heart. They showed that large external electrodes caused the greatest density of current through the heart for a given voltage.

TABLE I. ELECTRICAL FACTORS IN CLOSED CHEST CARDIAC FIBRILLATION AND DEFIBRILLATION

EXPERIMENT	WEIGHT (KG.)	SUBFIBRILLATION	FIBRILLATION	DEFIBRILLATION
6	17		0.5 sec. 110v.	0.15 sec. 250v.
7	34		0.5 sec. 135v.	0.15 sec. 550v.
8	14		0.5 sec. 110v.	0.15 sec. 350v.
9	22	0.5 sec. 110v.	0.5 sec. 135v.	0.15 sec. 650v.
10	19	1.0 sec. 85v.	0.5 sec. 135v.	0.15 sec. 550v.
11	16.2	0.5 sec. 135v.	0.5 sec. 160v.	0.15 sec. 550v.
12	24		0.5 sec. 160v.	0.15 sec. 550v.
13	19.8		0.5 sec. 160v.	0.15 sec. 550v.
14	14.5		0.5 sec. 160v.	0.15 sec. 550v.
29	20		0.5 sec. 135v.	0.15 sec. 550v.

Following the classic studies of Wiggers,[9] many workers have employed serial defibrillation in the open heart. However, Guyton and Satterfield found the average dog could usually be defibrillated through the unopened chest with a single shock of 160 volts, 60 cycle alternating current, and a shock of 220 volts was effective almost without fail. Our studies showed more consistent results with a single shock of higher voltage of 440 to 550 volts at 0.15 sec. This initial shock must be adequate to produce asystole, following which a faltering and then improving sinus rhythm develops (Fig. 1).

Effect of Electric Current on the Heart.—The dangers of producing burns with the use of high voltage on the exposed heart are apparent. Kaiser and coworkers,[10] using 130 to 230 volts at 0.1 and 0.25 sec., respectively, on the open heart, found microscopic burns in the myocardium of all dogs. However, only on those with the higher voltage and longer durations were the burns visible grossly and considered to be severe. Kirby and associates[11] reported similar findings. With a defibrillation shock of 220 volts, when the duration of the stimulus was increased from 0.1 to 0.5 sec., the hearts exhibited gross burns.

Although greater voltage is necessary when countershock is applied through the intact chest, it appears that the likelihood of damage to the heart is decreased.[12] Using a single countershock of 550 volts at 0.15 sec., no evidence of burns was seen on the skin, chest wall, or heart of any of our animals.

Three of the animals which survived 1 to 3 hours of fibrillation and subsequent defibrillation without sequelae were sacrificed from 2 to 3 months after the perfusion for examination of the heart. Gross examination revealed no evidence of scarring or healed burns of the epicardium or myocardium. However, histologic study[*] of random sections from the apex, septum, and base showed scattered focal and perivascular hemorrhages (*Figs. 2A and 2B*). In one of the hearts there were several areas of actual subendocardial infarction. In these lesions, there was gradual replacement of degenerating muscle fibers by proliferating granulation tissue. Occasional foreign body giant cells were seen. In the absence of surface burns and due to their subendocardial location, it was thought these changes were most likely the result of hypoxia. The heart of a fourth animal which died 24 hours after a 3 hour and 20 minute period of perfusion showed gross areas of subepicardial hemorrhage as well as focal interstitial hemorrhage between muscle fibers consistent with acute hypoxia.

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[*] Sections were kindly reviewed by Dr. K. P. Knudtson, pathologist, Veterans Administration Hospital, Seattle, Wash.

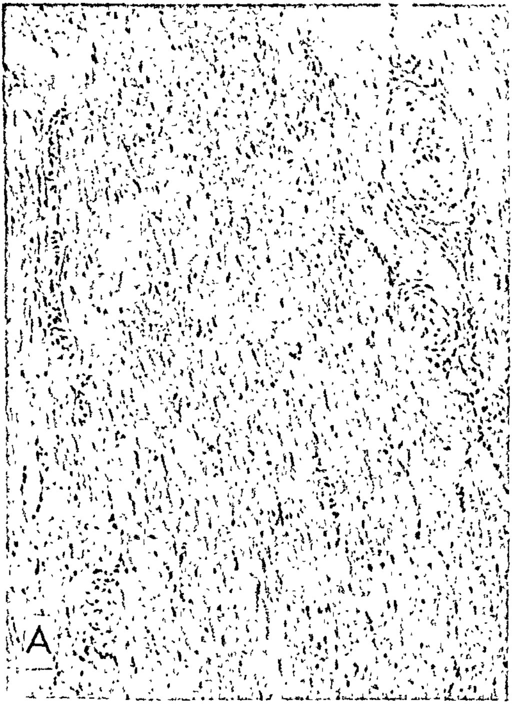

Fig. 2A.—(Photomicrograph) Dog No. 7 sacrificed at 2 months after perfusion. Heart grossly normal. Scattered focal and perivascular hemorrhage (×220; reduced ½).

Perfusion.—The vertical, all steel bubble oxygenator used for extracorporeal support in this study has been previously described.[13] The minimum perfusion rate necessary for prolonged support of the fibrillating heart and subsequent defibrillation and survival was unknown to us at the start of this work. From existing date, it was thought that flow rates varying from 45 to 70 c.c./Kg./min. should be adequate to maintain circulatory requirements. Based on the known values of cardiac output for dogs[14, 15] as the maximum desirable flow, and the report of Paneth, Lillehei, and co-workers[16] indicating the minimal flow requirement to prevent metabolic acidosis, we obtained moderate flow rates (Table II).

It was soon apparent that a compromise was necessary between desirable and obtainable flow rates. The principal factor limiting the rate of flow is the small size of the single peripheral venous catheter. The volume of venous return varied with the cross section of the catheter. The maximum obtainable venous return via the single peripheral femoral vein was found to average less

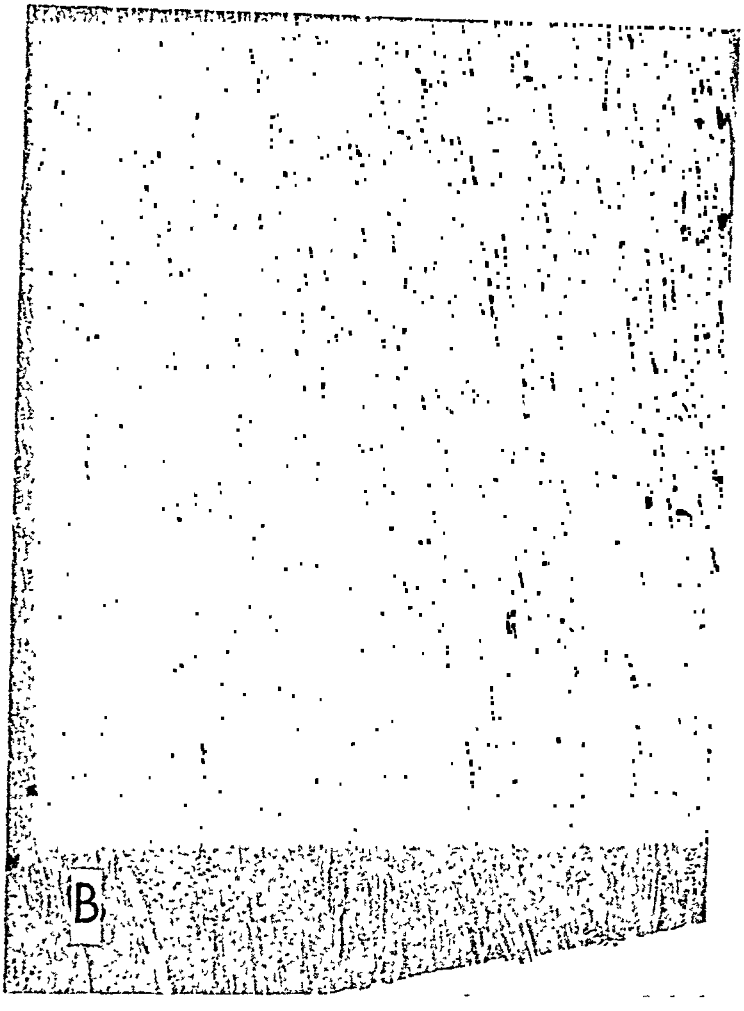

Fig. 2*B*.—Dog No. 8 sacrificed at 6 weeks. Heart grossly normal. Patchy degeneration of muscle fibers with gradual replacement by proliferating granulation tissue (×40; reduced ⅓).

TABLE II. PROLONGED VENTRICULAR FIBRILLATION

EXPERIMENT	AVERAGE PERFUSION RATE (ML./KG.)	DURATION	SURVIVAL
6	50 to 60	41 min.	Normal
7	40 to 44	42 min.	Normal
8	60 to 64	1 hr. 24 min.	Normal
9	50 to 54	51 min.	Normal
10	40 to 50	25 min.	Normal
11	70 to 80	1 hr. 46 min.	Normal
12	50 to 60	3 hr.	Normal
13	65 to 70	2 1/2 hr.	Normal
14	50 to 55	49 min.	Normal
29	45 to 55	3 hr. 20 min.	Died

than half the volume obtained by central cannulation and caval occlusion. Utilizing a double peripheral return from the jugular and femoral veins failed to add enough flow to warrant routine use. Gravity flow was unsatisfactory in maintaining whole body perfusion with peripheral cannulation and the heart

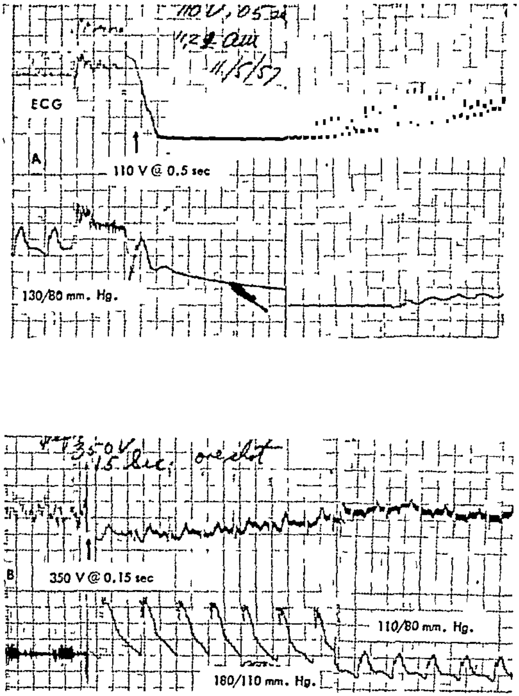

Fig. 3.—Experiment 8; 14 Kg. dog. *A*, Onset of ventricular fibrillation followed by 10 sec. of asystole (not shown). Fibrillatory pattern beginning with establishment of perfusion.
B, Successful initial defibrillation after 1 hour and 24 minutes. Immediate resumption of sinus rhythm and peripheral pressure pattern. Change from 180/110 mm. Hg to 110/80 mm. Hg represents blood volume adjustment.

in fibrillation. Within several minutes of the beginning of perfusion the available venous return would seek its own flow level. Right heart pressure usually stabilized at 6 to 9 cm. of water. Best results in reaching a steady state were achieved when extracorporeal perfusion was begun within 20 to 30 seconds of the onset of ventricular fibrillation (Fig. 3). Further delay in establishing circulation profoundly affected the available venous return. Whether the electric shock produced a peripheral vascular dilatation, allowing pooling in postarteriolar vessels, or the venous run-off permitted pooling in certain venous reservoirs, was not apparent. In the average run, a state of equilibrium was spontaneously established in which little or no adjustment of the pump speeds was necessary to balance the circulation during the 1- to 3-hour periods.

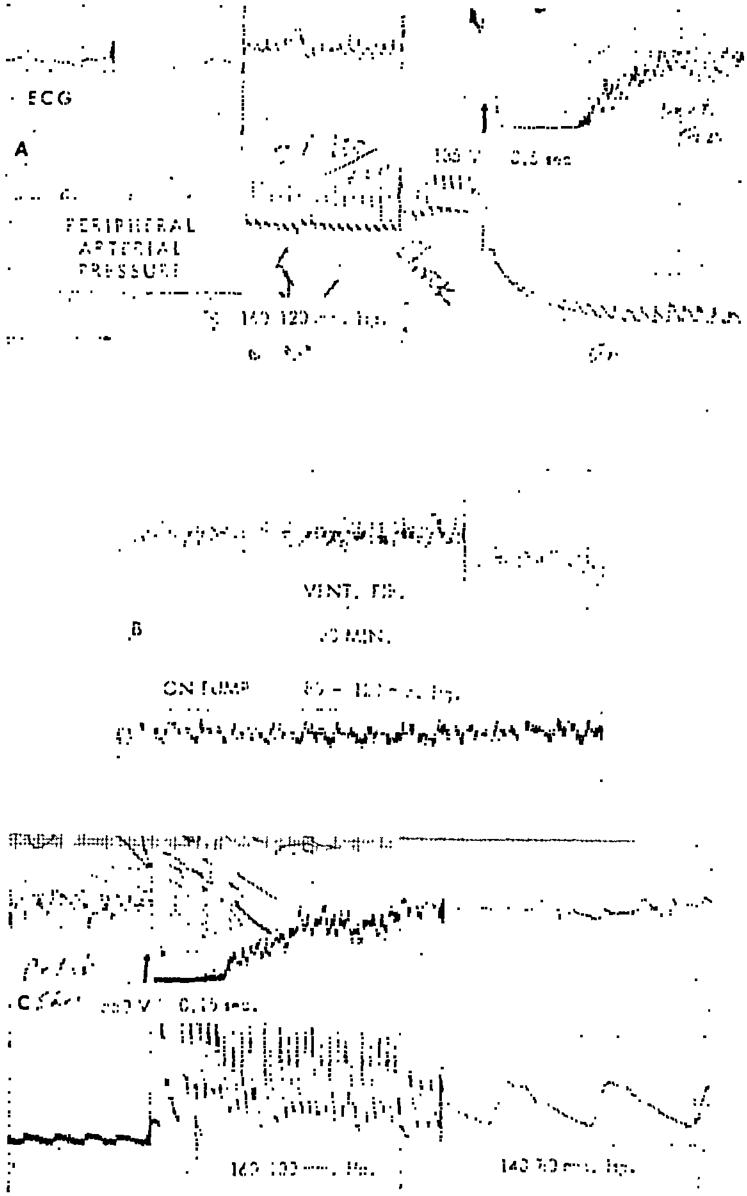

Fig. 4.—Experiment 7; 34 Kg. dog. *A*, Prefibrillation electrocardiogram and arterial pressure. Induction of ventricular fibrillation and prompt establishment of pump pattern on arterial tracing.

B, Constant fibrillatory pattern at 30 minutes. Mean arterial pressure from 80 to 120 mm. Hg at perfusion of 40 to 44 ml./Kg.

C, External defibrillation after 42 minutes. Postfibrillation electrocardiogram and blood pressure similar to prefibrillation values.

With flow rates, which were equivalent to one third to one half the animal's normal cardiac output, the mean arterial pressure varied from 80 to 100 mm. Hg (Fig. 4). Some animals exhibited a nearly normal blood pressure at these low flow rates, whereas others maintained levels from 60 to 80 mm Hg It was found that the principal determinant of mean blood pressure was not flow rate but total peripheral resistance[1]

Biochemical Changes—The blood values incident to extracorporeal support with this particular oxygenator were reported previously Detailed studies of blood chemistry or clotting factors were not a part of this work For evaluation of the metabolic state after prolonged perfusion venous pH was determined at intervals during several of the experiments The results are given in Fig 5 It may be seen that in most runs the venous pH remained within a fairly constant range A cumulative acidosis was occasionally seen and usually responded to a slight increase in oxygen flow or perfusion rate, or both In the last animal of the series, an effort was made to extend the perfusion period beyond 3 hours At 3 hours and 20 minutes although initial defibrillation was successful, the animal expired in 24 hours Review of the pH revealed a marked acidosis with the lowest value in the series The absence of cerebral activity prior to death suggested that the low flow rate resulted in cerebral hypoxia

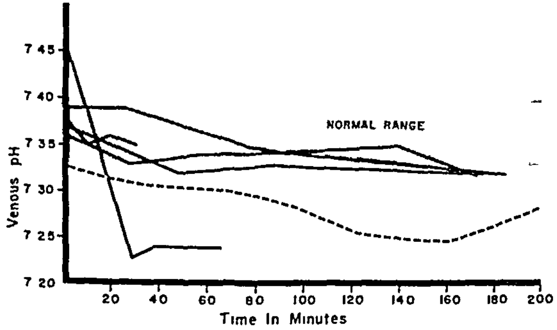

Fig 5—Graph of pH values during six fibrillation experiments with total body perfusion Broken line indicates acute acidosis of the single nonsurviving animal

It has been reported that the fibrillating heart loses potassium In the isolated dog heart perfused with Locke's solution, Kehas and Hooker[18] noted the maximum value for potassium at ½ to 1 minute after the onset of fibrillation Values at 3 to 4 minutes often showed a return to prefibrillation levels In our studies, isolated determinations of serum potassium taken at intervals during several 1 and 2 hour fibrillation runs were unchanged from control values

Cardiac Activity During and After Ventricular Fibrillation—Prior to the development of extracorporeal pump oxygenators, no direct measures were available for the support of coronary circulation during ventricular fibrillation other than cardiac massage Observation of the electrocardiogram following the onset of ventricular fibrillation shows a fine, rapid, tremulous pattern of about 400 to 500 frequencies per minute Without massage, direct coronary perfusion or oxygenator support, the fibrillation pattern disintegrates, with progressive anoxia. After 3 to 5 minutes, the fine wave gives way to a slow, coarse wave of low amplitude, terminating in complete arrest. Experimental studies by Senning[19] with prolonged fibrillation in the normothermic, open chest animal showed that the fibrillatory pattern was unchanging during oxygenator support. Our findings were similar to those of Senning in that the wave pattern was consistent as long as mechanical difficulties in the system did

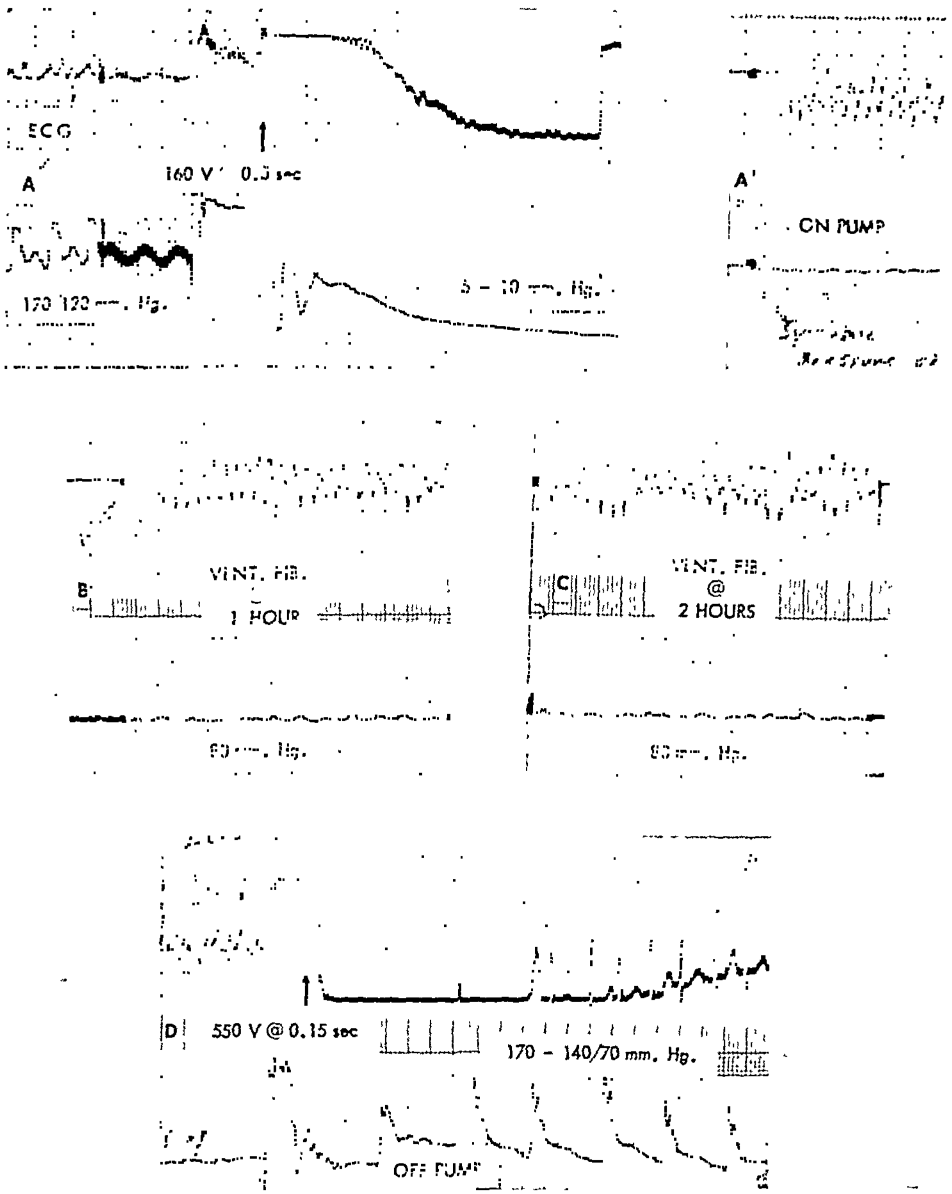

Fig. 6.—Experiment 12; 24 Kg. Dog. *A*, Closed chest induction of ventricular fibrillation. Ten to 12-second interval (not shown) prior to appearance of frank fibrillation and peripheral pressure (pump pattern) *A'*.

B, Essentially unchanging nature of ventricular fibrillation from *C*, hour to hour, suggesting satisfactory myocardial oxygenation. Mean arterial pressure 80 mm. Hg, perfusion 50 to 60 ml./Kg.

D, Electric defibrillation after 3 hours of extracardiac substitution. Countershock is followed by asystole and gradual resumption of sinus rhythm and prefibrillatory pressure tracing.

not intervene (Fig. 6). Countershock was not satisfactory for defibrillation unless threshold intensity was sufficient to produce asystole. Step increases in voltage were occasionally necessary in the larger animals. Following a brief asystole, a bradycardia with varying degrees of block was seen. During the subsequent 5 to 10 minutes, the rhythm gradually resumed the prefibrillatory pattern. In the surviving animals, systolic pressure was maintained at nearly normal levels without support. Ventilatory support was also unnecessary if cerebral centers had been adequately oxygenated. Spontaneous and effective ventilation began soon after discontinuance of the oxygenator. An effort was made to restore the animal to as nearly a normovolemic state as possible at the completion of the run. This was done by regaining the blood level in the oxygenator and observing the effect of hyper- or hypovolemia on the arterial pressure amplitude.

An interesting and unexpected finding was the presence of a regular atrial wave during the entire period of ventricular fibrillation. Although the atria would fibrillate when mechanically stimulated in the exposed heart, spontaneous rhythm was immediately resumed when the atria were released.

DISCUSSION

In considering the deliberate use of ventricular fibrillation in human beings for open heart surgery, Glenn[20] has pointed out that coronary flow is uncontrolled and spontaneous defibrillation may occur with a well-oxygenated heart. Although we have not seen spontaneous defibrillation of the heart in normothermic dogs, Juvenelle,[21] Swan,[22] Bigelow[23] and others observed both spontaneous fibrillation and defibrillation during cooling and rewarming of the hypothermic dog.

Senning,[19] in 1951, was perhaps the first deliberately to induce ventricular fibrillation during total body perfusion. This suggestion was advanced in an effort to obtain cardiac standstill and to avoid coronary or cerebral air embolism during intracardiac surgery. In a subsequent monograph, Senning reported on many aspects of ventricular fibrillation. Using a modified Crafoord-Andersson-Björk disc oxygenator and central cannulation in the open chest animal, he was able to support the normothermic fibrillating heart for prolonged periods with successful defibrillation.

In a similar study but utilizing hypothermia with peripheral connection of the femoral vessels to the oxygenator, Juvenelle and co-workers[21] were able to support the fibrillating heart up to periods of 3 hours with subsequent defibrillation. Both Senning and Juvenelle were able to demonstrate that this arrhythmia is innocuous providing there is proper cardiac oxygenation.

In the absence of a massaging action by the contracting muscle, coronary flow may fluctuate to below or above normal values. Studies of oxygen consumption during fibrillation have been contradictory. Senning reported no significant difference in the fibrillating state as compared to the normally beating heart. On the other hand, Paul and co-workers[24] found slightly less oxygen utilization, while Green and Lorber[25] demonstrated an increased oxygen consumption.

The ease of defibrillation, both experimentally and clinically, while the heart is supported by the pump-oxygenator suggests the metabolism of the fibrillating and contracting heart is similar. As the oxygen requirement is certainly greater during fibrillation than for the heart in chemical or anoxic asystole, successful defibrillation and normal survival after prolonged extracorporeal substitution may indicate the effectiveness of a particular oxygenator and perfusion rate in meeting myocardial and cerebral demands.

SUMMARY AND CONCLUSIONS

1. Prolonged substitution for the fibrillating ventricles has been accomplished in the closed chest animal by total body perfusion with a bubble oxygenator.
2. Defibrillation with electric countershock and restitution of sinus rhythm could be successfully achieved after long periods of fibrillation, providing the oxygen requirement of the myocardium is satisfied.
3. Coronary perfusion is necessary for myocardial support during the fibrillatory state.
4. Since deliberate ventricular fibrillation eliminates both the greater and lesser circulation, successful total body perfusion requires an efficient pump-oxygenator.
5. The controlled fibrillatory state is a useful experimental method for the study of hemodynamic phenomenon in the central circulation and the production of partial or total cardiogenic shock.

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COMPARATIVE EFFECT OF 15 PER CENT POTASSIUM CHLORIDE AND 30 PER CENT POTASSIUM CITRATE IN RESUSCITATION FROM VENTRICULAR FIBRILLATION FOLLOWING ACUTE MYOCARDIAL INFARCTION

An Experimental Study

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THERE have been relatively few experimental observations on resuscitation of the heart following acute cyocardial infarction.[10, 11, 14, 15, 17] Previous work by one of us (F. W.) has demonstrated the relative effectiveness of 15 per cent potassium chloride in converting ventricular fibrillation to ventricular standstill in normothermic laboratory animals following acute myocardial infarction.[14] The restoration of coordinated cardiac beating occurred in all of these animals with variable difficulty. Other investigators have shown that 15 per cent potassium chloride would promptly convert ventricular fibrillation to ventricular standstill in deeply hypothermic laboratory animals without acute myocardial infarctions[13]; in these studies restoration of cardiac beating was apparently accomplished with greater facility using concentrated Ringer's lactate and molar sodium lactate.

Interesting case reports in the recent literature give dramatic testimony to what may be accomplished with active resuscitation attempts.[2, 5, 6, 8, 12] We believe as others[1, 18] that many deaths from acute myocardial infarction are "electrical" rather than "muscular," and it is this belief, supported in part by earlier observations in the experimental animal, that provided the impetus for the present study.

The purpose of this paper is to report on the relative efficacy of 15 per cent potassium chloride and 30 per cent potassium citrate in converting ventricular

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fibrillation to ventricular standstill following acute myocardial infarction in the experimental animal. The ultimate aim of this effort is to standardize a procedure which can be instituted with sufficient ease and frequency to justify organized and vigorous efforts in attempts to resuscitate patients dying from coronary artery disease.

METHOD AND MATERIAL

Forty mongrel dogs weighing between 15 and 40 pounds were studied. The typical animal was lightly anesthetized with pentobarbital sodium and given positive pressure air and/or oxygen through an endotracheal tube, both mechanical respirators and bagging procedures were employed. Each experiment was performed utilizing strict aseptic technique. The chest was opened with a transsternal incision to enhance exposure. Hemostasis was carefully maintained. The femoral artery was cannulated for the withdrawal of blood specimens (pH, serum electrolyte and chemical determinations) and the recording of arterial blood pressures. Continuous electrocardiograms and simultaneous arterial pressures were recorded on the Sanborn Twin Visocardiette. The femoral vein was cannulated for the administration of various drugs. The anterior descending branch of the left coronary artery was ligated with a 1-0 silk suture 0.5 cm. distal to its bifurcation. Electrocardiographic tracings were followed until the changes characteristic of an acute myocardial infarction were observed. Subsequently, ventricular fibrillation either (a) occurred spontaneously within 10 to 15 minutes following the acute infarction or (b) was induced by electric shock (50 to 150 volts) applied directly to the heart, utilizing a defibrillator. Untreated ventricular fibrillation occurring under these circumstances was irreversible.

Immediately after the onset of ventricular fibrillation 20 animals were treated with 15 per cent potassium chloride to induce ventricular standstill and 20 animals were given 30 per cent potassium citrate. The effect of the intracardiac administration of hypertonic potassium (into one or both ventricles) was compared to the administration of the solutions into the proximal portion of the cross-clamped aorta and into one or both ventricles with the aorta cross-clamped.

Following the administration of potassium, slow cardiac massage (30 to 50 per minute) was initiated until the electrocardiogram demonstrated conversion of the ventricular fibrillation to ventricular standstill. The effectiveness of blood flow in the large arteries could roughly be gauged by the pressure recordings from the femoral artery. With the onset of ventricular standstill, cardiac message was speeded to 70 to 100 times per minute, and one molar sodium lactate was administered intravenously and occasionally in small amounts (up to 20 c.c.) into the heart. The total amount administered ranged from 30 to 350 c.c. (see Table I). In each animal studied repeated episodes of ventricular fibrillation were terminated with hypertonic potassium chloride or potassium citrate, depending upon which agent was being studied.

with that particular animal. Restoration of cardiac beating following each episode of ventricular fibrillation in the same animal was approached, utilizing a method similar to that employed for the initial episode. Where cardiac message or spontaneous cardiac beating appeared to be unable to maintain a satisfactory level of arterial pressure, varying concentrations of intravenous l-norepinephrine were administered. Following successful restoration of cardiac beating and return of the blood pressure to near normal levels, the chest was closed with wire stay sutures and silk, and the animals were gradually weaned from the artificial respirator. The femoral catheters were subsequently removed, 10 to 15 minutes following the appearance of normal sinus rhythm associated with a normal or near normal arterial pressure. Postoperative animals were given intramuscular crystalline penicillin and streptomycin. No intravenous fluids were administered in the postoperative period; the animals were, however, allowed to eat and drink ad libitum. Frequent samples of blood for pH and serum electrolytes were analyzed using standard laboratory procedures to compare the electrolyte, chemical, and pH changes with 15 per cent potassium chloride and 30 per cent potassium citrate induced arrest.

RESULTS

Ventricular fibrillation, complicating acute myocardial infarction, in the experimental animal represents an irreversible terminal mechanism.

Changes in Arterial pH, Serum Electrolytes in Chemistry.—

1. *15 per cent potassium chloride:* Two 5 to 10 c.c. intracardiac injections of 15 per cent potassium chloride were given to terminate each episode of ventricular fibrillation. The total amount of potassium chloride administered was equally divided between the right and left ventricular cavity when intracardiac injection was studied. When the aorta was cross-clamped the total amount was given into the proximal portion of the aorta. It appears that conversion from ventricular fibrillation to ventricular standstill was accomplished with equal facility with both methods of administration. The total amount of potassium chloride required to induce ventricular standstill, following each episode of ventricular fibrillation, averaged 15 c.c. (see Table I).

Electrolyte and pH changes: The serum potassium concentrations attained their maximum immediately following the administration of potassium chloride. These very high levels (required to produce ventricular standstill) ranged from 8.4 mEq. per liter to 40.5 mEq. per liter. With the restoration of cardiac beating, high serum potassium levels fell precipitously, usually within 5 to 15 minutes, to levels ranging from 4.8 mEq. per liter to 10.8 mEq. per liter. As the effectiveness of cardiac beating improved, elevated serum potassium concentrations gradually returned to levels near normal or only slightly higher than normal (6.9 mEq. per liter).

Subsequent episodes of ventricular fibrillation, terminated with potassium chloride, were followed by an abrupt elevation in the serum potassium, usually to a concentration slightly more than that observed following termination of the initial episode The serum chloride level showed a marked increase as a result of the hypertonic potassium chloride arrest (paralleling the serum potassium) The serum sodium concentration gradually increased following the intravenous administration of molar sodium lactate and reached its zenith toward the end of the experiment Maximum serum sodium levels ranged from 138 mEq per liter to 216 mEq per liter The serum calcium level decreased slightly throughout the experiment, the low range being 8 2 mg per cent to 8 7 mg per cent The carbon dioxide combining power decreased abruptly following induced cardiac arrest (Fig 1*B*) and subsequently returned to near normal levels The average fall was 14 mEq per liter There was no significant change in the serum magnesium concentration The arterial pH fell significantly The most abrupt fall occurred immediately after the administration of potassium chloride and in general coincided with the onset of ventricular standstill Subsequently, the blood pH either remained low in spite of the administration of molar sodium lactate, or was decreased further by an unknown, apparently paradoxical, mechanism The average fall of the arterial pH was 0 32 Fig 1*A* and 1*B* show the significant mean changes in the serum sodium potassium carbon dioxide combining power and arterial pH occurring during the procedure

2 *30 per cent potassium citrate* In 20 animals studied with 30 per cent potassium citrate arrest the most effective method of administration appeared to be equal division of the total amount into both the right and left ventricle The total amount of potassium citrate required to induce ventricular arrest (standstill) ranged from 4 c c to 32 c c

Electrolyte and pH changes In general the changes in the serum electrolytes corresponded to those observed following hypertonic potassium chloride with several exceptions The serum chloride level remained essentially unchanged following potassium citrate arrest, and the increase in the serum potassium level was never as marked as that observed following potassium chloride arrest The maximum serum potassium concentrations ranged between 10 1 and 19 5 mEq per liter The carbon dioxide combining power decreased slightly throughout the procedure (as with potassium chloride), and the serum calcium either remained unchanged or decreased slightly, following, and probably as a result of, the intravenous sodium lactate therapy [4] There was no apparent change in the serum magnesium Comparative mean electrolyte and pH changes are shown in Figs 1*A* and 1*B*

Effect of 15 Per Cent Potassium Chloride and 30 Per Cent Potassium Citrate on Resuscitation From Ventricular Fibrillation —

The mean number of episodes of ventricular fibrillation using hypertonic potassium chloride arrest was 5, with hypertonic potassium citrate arrest, this was reduced to 3

In 39 of the 40 animals studied, the intracardiac administration of both hypertonic potassium solutions converted the ventricular fibrillation to ventricular standstill; one animal died an anesthetic death. In general, hypertonic potassium citrate appeared to be more effective in that ventricular standstill occurred more promptly and with greater facility; the tendency to develop multiple episodes of ventricular fibrillation was reduced with 30 per cent potassium citrate (Table 1).

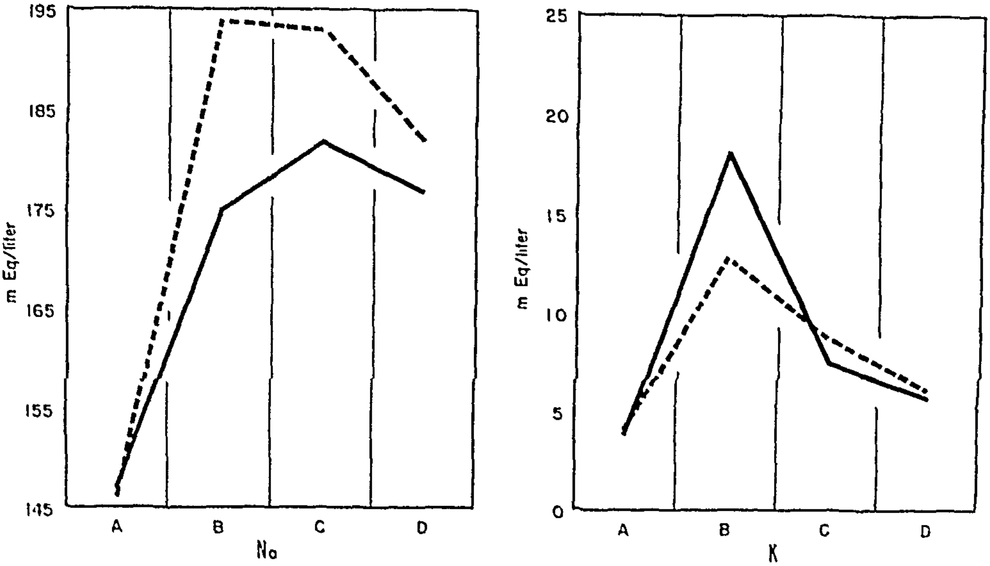

Fig. 1*A*.— ——— K Cl 15%. - - - - - K citrate 30%. *A*, Before opening chest. *B*, Cardiac arrest. *C*, Restoration of cardiac action. *D*, End of procedure.

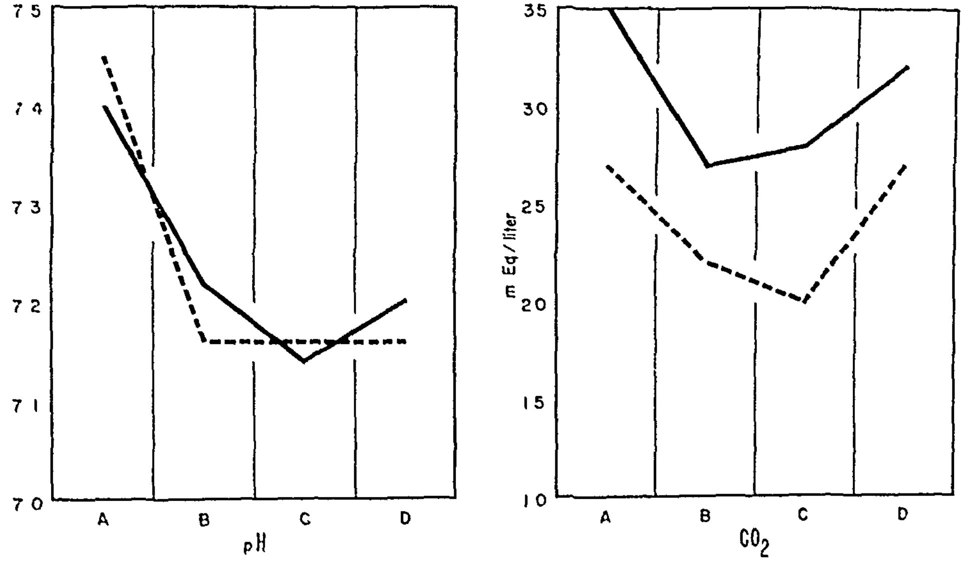

Fig. 1*B*.— ——— K Cl 15%. - - - - - K citrate 30%. *A*, Before opening chest. *B*, Cardiac arrest. *C*, Restoration of cardiac action. *D*, End of procedure.

In 19 of the 40 animals, we were able to restore the heart to normal sinus rhythm and the blood pressure to normal or near normal ranges (Fig. 2).

TABLE I

TYPE OF K SOLUTION USED	AVERAGE AMOUNT K TO TERMINATE EACH EPISODE OF VENTRICULAR FIBRILLATION	AVERAGE NO OF EPISODES OF VENTRICULAR FIBRILLATION	AVERAGE DURATION OF INITIAL EPISODE OF VENTRICULAR FIBRILLATION	AVERAGE AMOUNT MSL* AFTER EACH EPISODE OF ARREST
15% KCl	15 c.c.	5	3 min	100 c.c.
30% K Citrate	5 c.c.	3	50 sec	40 c.c.

*Molar sodium lactate

Twelve of these subsequently died while the chest was being closed Six of the 12 animals died as a result of the following difficulties. hemorrhage (1 dog); apparently irreversible damage to the respiratory center (manifested by an inability to resume breathing spontaneously [2 dogs]); trauma and laceration of the myocardium incident to massage (2 dogs), and inadequate pulmonary ventilation following closure of the chest (1 dog) Seven animals survived the entire procedure, living from 1 hour to 6 months The hearts of these animals were subsequently examined grossly and microscopically.

In the remaining 20 animals, normal sinus rhythm never became re-established. In many of these, an auriculoventricular nodal rhythm or a transient return to normal sinus rhythm was observed, following which repeated episodes of ventricular fibrillation signified the end of the experiment

Pathologic Examination of the Heart.—

Pathologic examination of the hearts at varying periods of time following successful cardiac resuscitation showed either the change of an acute or chronic myocardial infarction In an animal sacrificed after surviving 6 months, the large anterolateral myocardial infarction visualized during the acute procedure had healed so that only the residual changes of a small transmural area of fibrosis in the anterior wall of the left ventricular myocardium was demonstrated histologically

DISCUSSION

Previous experimental work had demonstrated that in spite of an acute, apparently extensive, myocardial infarction, 3 out of 4 animals studied with terminal ventricular fibrillation were ultimately restored to a supraventricular rhythm with normal or near normal blood pressures[11] In the present study, performed utilizing strict aseptic technique, earlier observations (using hypertonic potassium chloride) were repeated and compared with hypertonic potassium citrate arrest From this study it appears that 30 per cent potassium citrate is superior to 15 per cent potassium chloride in converting ventricular fibrillation to cardiac standstill Induced potassium citrate arrest resulted in less severe potassium intoxication which appeared to be more readily reversed by treatment with molar sodium lactate[3] Apparently undesirable hyperchloremia observed with potassium chloride was not present when potassium

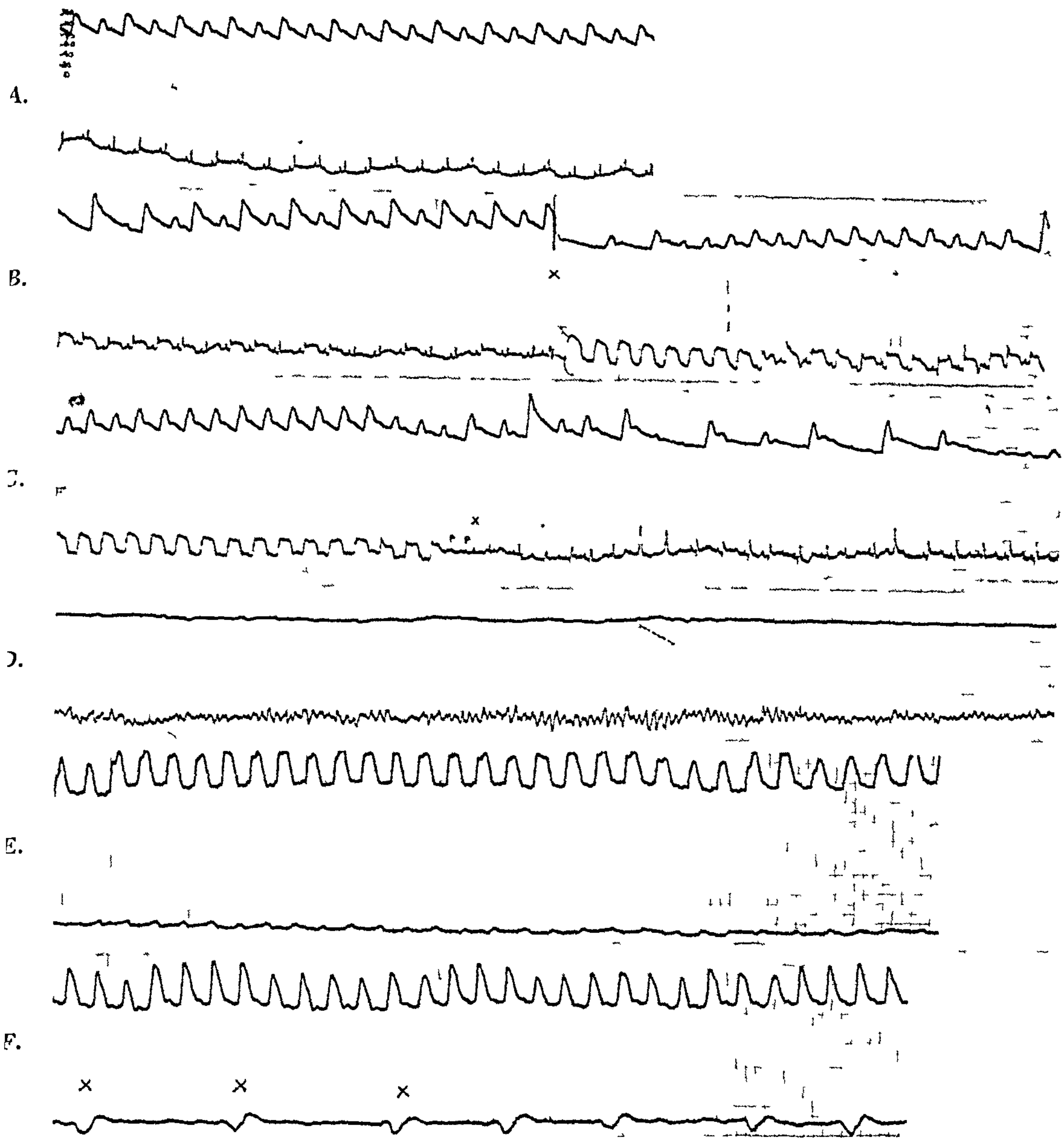

Fig 2.—*A*, Control (Lead II), simultaneous arterial pressure is 120/80 mm Hg

B, First half of record taken 10 minutes after ligation of the anterior descending coronary artery shows RS-T segment elevation of the type seen in acute coronary artery occlusion The arterial pressure is 124/60 mm Hg From *X* until the end of the record note the characteristic high take-off of the RS-T segment accompanying the acute myocardial infarction The pressure has fallen to 84/44 mm Hg

C, Thirty minutes after acute coronary ligation note the conduction disturbance at *X*

D, Forty minutes following acute coronary artery occlusion at 2 30 P M, ventricular fibrillation was induced by applying electrodes to the ventricles and administering a single 50-volt electric shock

E, Forty-five seconds after 3 c c of 30 per cent potassium citrate had been given into both ventricles, ventricular fibrillation has been converted to ventricular standstill Cardiac massage was started (at a rate of 100 per minute) Note the apparent effectiveness of arterial flow as recorded by a catheter in the femoral artery

F, Three minutes after ventricular standstill, note the onset of electrical activity at *X* with widened, bizarre QRS complexes Intravenous molar sodium lactate has been started at a rate of 5 c c per minute

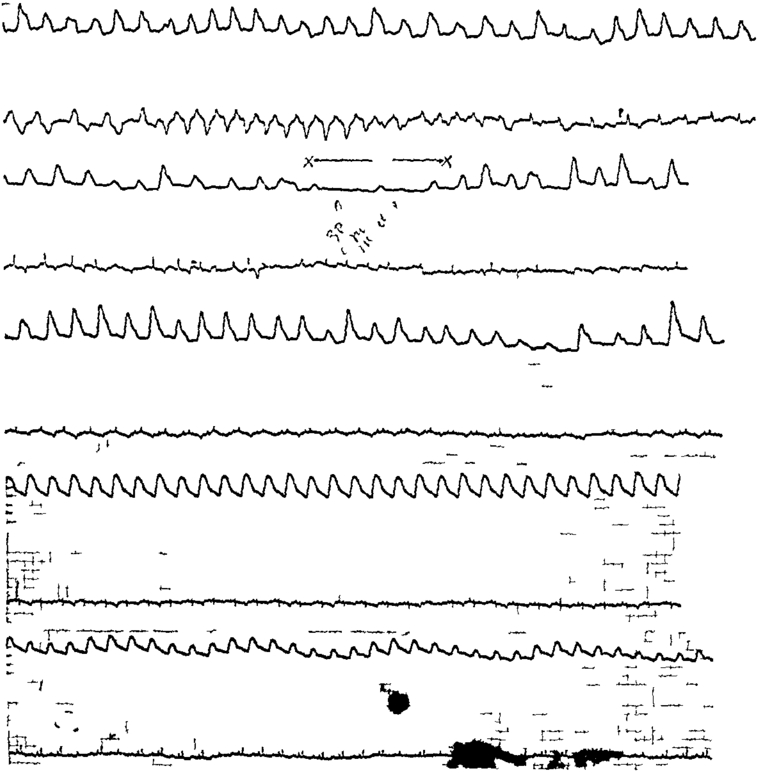

Fig 2—Cont'd *G* Five minutes after *F* following a total of 40 c c of molar sodium lactate there is progressive narrowing of the QRS complexes and a suggestion of restoration of auricular activity (*P*) Cardiac massage has been continuous

H Twelve minutes after ventricular standstill the QRS complexes have narrowed to a near normal width Note the effects (X) on the arterial pressure of discontinuing cardiac massage

I Fifteen minutes after induced ventricular arrest there is a return to normal sinus rhythm The arterial pressure is being supported with a very slow intravenous drip containing 1 ampule of l norepinephrine diluted in 40 c c molar sodium lactate

J Twenty five minutes after ventricular standstill there is spontaneous effective cardiac beating (without massage) The arterial pressure is maintained at 110/60 mm Hg without massage or drugs The QRS complexes are low in amplitude The T wave is inverted and the QT interval appears prolonged for the heart rate (approximately 116 per minute)

K One hour and thirty minutes after death in ventricular fibrillation the arterial pressure is 100/60 mm Hg The chest has been closed and the animal has resumed spontaneous breathing citrate was used. The paradoxical observation that the arterial pH continued to remain low with both hypertonic potassium solutions, even after restoration of effective cardiac beating, is difficult to understand; particularly after rather large amounts of a mild alkalizing solution (sodium lactate) had been given. In the hope of clarifying this, we are at the present time studying the carbon dioxide tension in the plasma.

Changes in the serum calcium probably reflected the use of varying amounts of sodium lactate intravenously as has been previously noted.[4] This decrease in the serum calcium would appear to increase the cardiotoxic effect of even a slight elevation in the serum potassium concentration, and we should like to be able to prevent this. Earlier studies have suggested that calcium is useful in hearts arrested by potassium.[9, 16] In our experience, however, it seemed difficult to quantitate the amount of calcium which was helpful and the danger of overdosage (recurrent ventricular fibrillation) limited its usage.

Blood Pressure Changes.—The persistent acidosis might explain the tendency for some of the animals to remain mildly hypotensive even following the return of a normal sinus mechanism (electrocardiographically) with apparently forceful, effective, mechanical cardiac contractions. In these animals, the combination of l-norepinephrine and molar sodium lactate often successfully restored the blood pressure to normal or near normal levels. One might anticipate such a reaction as a result of the observation that alkalosis appears to enhance the effectiveness of intravenous vasopressor agents.[7]

In the animal surviving longest (6 months), an interesting, perhaps superfluous, observation is the fact that this dog delivered a litter of 4 apparently normal pups approximately 5 months after successful cardiac resuscitation.

From our observations it appears that one can anticipate occasional long-term survival animals with a standardized resuscitation attempt utilizing 30 per cent potassium citrate to induce ventricular arrest and a combination of cardiac massage, molar sodium lactate, and l-norepinephrine. Further studies have been initiated to elaborate on these observations.

SUMMARY

Thirty per cent potassium citrate was more effective than hypertonic potassium chloride in converting otherwise irreversible ventricular fibrillation to ventricular standstill in normothermic laboratory animals with acute myocardial infarction. Continuous electrocardiograms and arterial pressures were recorded throughout each procedure and serial electrolyte, chemical, and pH changes were studied and are discussed.

Of the 40 animals included in this report, 7 survived and were observed from hours to months following successful cardiac resuscitation.

Some of the problems encountered in this study are presented. The need for further experimental observations in organized resuscitative attempts following death from acute myocardial infarction is stressed.

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TIME STUDIES OF ACUTE, REVERSIBLE, CORONARY OCCLUSIONS IN DOGS

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The surgical management of coronary occlusion has been directed toward relief of chronic myocardial ischemia by means of a number of revascularization procedures. In the past, the indirect approach to revascularization has predominated with grafting of various tissues onto the myocardium[1, 2] (omentum, lung, pectoral muscle), implantation of systemic arteries into the heart musculature,[3] abrasion of the epicardium,[4] and arterialization,[5] or merely constriction of the coronary sinus, to name a few. Lately, the direct attack on the constricting lesion, whether by endarterectomy,[6] or by excision and replacement of the diseased segment,[7] has made its appearance both clinically and experimentally.

Once the feasibility of the direct approach to the well-established occlusion is accepted, it takes but an additional step to consider the applicability of similar direct measures on the acutely obstructing process, that is, the emergency surgical treatment of the acute coronary occlusion.

An essential factor in establishing the effectiveness of such a policy would be to ascertain the available time during which emergency relief of an acute complete occlusion would result in preventing death of the myocardium. Should this time be commensurate with the interval needed for the rendering of a correct clinical diagnosis, transportation of the patient to a surgical facility and the performance of an emergency operation, such a policy would have a rational basis.

In order to determine the critical period during which emergency relief of the complete occlusive process would be curative, the following experiments were undertaken.

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METHOD

Mongrel dogs weighing between 12 and 20 Kg. were anesthetized with intravenous Pentothal, intubated, and attached to a mechanical respirator. One hundred per cent oxygen was administered throughout the procedure. The left common carotid artery was cannulated and continuous blood pressure was recorded thereby.

A left thoracotomy was performed through the fifth intercostal space. After incising the pericardium and securing it to the chest incision, the anterior descending branch of the left coronary artery was dissected free in its proximal 0.5 to 1.5 cm., care being taken to avoid trauma to its branches or to the accompanying veins. A No. 2 braided silk ligature was then passed around the artery and both ends were threaded through a short length of soft plastic tubing in order to provide a tourniquet.

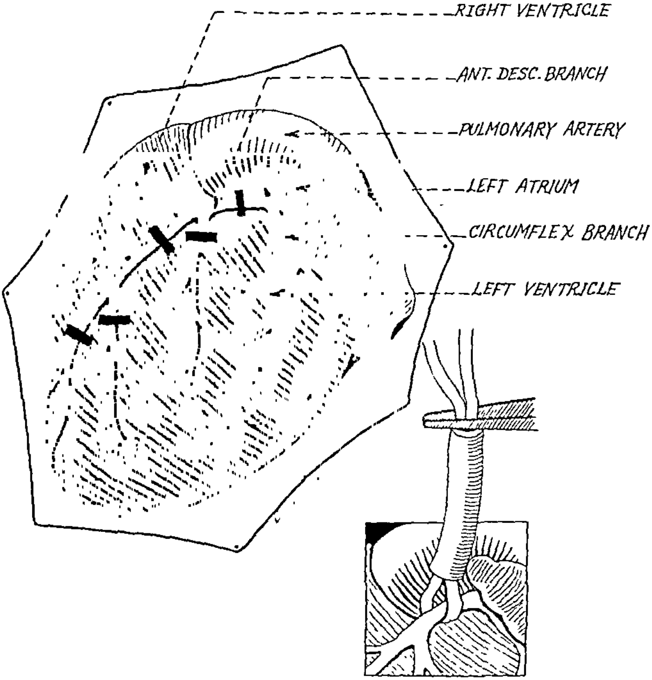

Fig. 1.

In 7 of the dogs the same procedure was employed at other sites along the course of the anterior descending artery or its two main branches, as indicated in Fig. 1.

The tourniquet was then tightened, occluding the involved portion of the artery completely, as evidenced by distal collapse of the vessel and appearance of a cyanotic area corresponding to its distribution. Stimulation of the heart was avoided during the occlusion period, but undue drying of the myocardial surface was prevented by moistening it with warm saline solution.

A record was kept of the myocardial action and color, blood pressure, and condition of the corneal reflex. After a definite period, the occlusion was terminated, the silk ligature was removed, and the pericardial and chest incisions were closed. If fibrillation occurred during the period of occlusion the tourniquet was released and removed. Massage and electrical defibrillation were instituted and, after the return of a normal heart rate and rhythm and stabilization of blood pressure, the operation was terminated in the manner previously described.

Electrocardiogram recordings of the three standard leads were obtained before opening the chest, during and after occlusion, and after chest closure. They were repeated at the time of sacrifice which varied between 48 hours and 14 days after the operation.

At sacrifice, the heart was excised and examined grossly. Twenty hearts were examined microscopically, noting the condition of the myocardium supplied by the temporarily occluded artery, and examining the vessel itself for evidence of permanent damage or of postoperative thrombotic phenomena. The latter were reported only once.

RESULTS

As described under Method, the area of heart muscle supplied by the occluded vessel became cyanotic within 2 to 3 minutes after starting the occlusion. As time went on, the cyanosis deepened and the affected area became sharply delineated from the surrounding normal myocardium. In some of the longer occlusions (over 45 minutes), paradoxical movement of the cyanotic area was observed with bulging during systole. After release of the occlusion, the distal portions of the artery were seen to fill readily from above and the cyanotic discoloration disappeared gradually.

Fibrillation.—Fourteen (46.7 per cent) out of 30 dogs exhibited ventricular fibrillation. In 9 (30 per cent), fibrillation appeared during the occlusion at which time the latter was terminated. The time of onset of fibrillation averaged 9 minutes and 36 seconds (range—from 1 to 20 minutes). Five (16.7 per cent) hearts fibrillated upon release of the constricting ligature after a predetermined period of occlusion. One dog died. The rest were successfully defibrillated with application of cardiac massage and one or more electric shocks.

Electrocardiographic findings during occlusion were predominantly T-wave and RS-T segment changes. During occlusion, inversion of the T wave occurred frequently, but in 3 dogs, with inverted T waves before occlusion, we observed positive deflections shortly after occlusion. Marked shifts of RS-T segments were noted on 11 dogs, with depression in 5 and elevation in 6. In the majority these changes disappeared and the deflection returned to the preoperative state upon the release of the constricting ligature.

Electrocardiographic changes at sacrifice (2 to 14 days after operation) in all dogs with temporary occlusion periods over 45 minutes, showed evidence of severe coronary insufficiency or of definite anterolateral infarction. In animals with shorter occlusive periods the findings were minimal or absent with the exception of one dog with a 12 minute occlusion in which changes suggestive of myocardial infarction were reported. This animal had suffered from ventricular fibrillation and received multiple electric shocks to restore normal rhythm. At autopsy there was hemorrhage around the area of ligation but no microscopic evidence of infarct. The pathologic changes were probably caused by the trauma incidental to the resuscitative measures.

Pathologic Changes Following Temporary Ligation.—Twenty hearts were examined 2 to 14 days after operation. Five dogs undergoing occlusion of branches of the anterior descending coronary artery for 30 minutes did not show gross or microscopic evidence of myocardial involvement.

In 15 dogs there were definite myocardial changes as follows: All hearts subjected to occlusion of the anterior descending branch of the left coronary artery for 45 minutes or more showed myocardial necrosis with varying degrees of round cell infiltration or fibrous replacement. With one exception, the coronary vessels were patent at the time of sacrifice. In this animal (No. 27) the anterior descending artery showed partial occlusion with thrombus at the site of temporary ligation. This obstruction had narrowed the lumen of the vessel to 25 per cent of normal. Microscopic findings in dogs undergoing occlusions of 30 minutes' duration or less were minimal and were limited to hemorrhages and inflammatory cell infiltration. Invariably these changes occurred in dogs with ventricular fibrillation at some time during the procedure and were undoubtedly the result of trauma during cardiac massage and electric shock.

Pericarditis was reported in 7 dogs but appeared unrelated to myocardial damage.

DISCUSSION

Our operative, electrocardiographic and pathologic findings parallel the reported experiences of others with this type of vascular insult to the myocardium.

The incidence of ventricular fibrillation in this group (46.7 per cent) is lower than has been reported by Bakst,[8] Orias[9] or Litvak[10] (60.6 per cent to 78.6 per cent) but higher than the 10 per cent encountered by Chardack[11] who also used 100 per cent oxygen given by an artificial respirator during the procedure.

The phenomenon of fibrillation at the time of re-establishment of circulation has been observed by others (Blumgart[12] and Sewell[13] and their co-workers) and has been explained by Beck[14] on the basis of a sudden change in oxygen potential of adjacent areas of myocardium. There was only one death from this arrhythmia attesting to the efficacy of prompt cardiac massage and electric defibrillatory shock.

The electrocardiographic findings for this type of occlusion have been extensively studied and the typical T wave and RS-T segment changes have been emphasized by Bayley and associates,[15] Harris and Hussey,[16] Rakita,[17] and Kimura.[18] It would be interesting to determine the changes incidental to partial occlusion in objectively graded degrees, and by the same method to determine the sequelae of partial occlusions from a pathologic standpoint inasmuch as, in clinically encountered occlusion, partial obstructions of one or more segments of an artery are probably very frequent.

The pathologic evidence shows that a complete occlusion of a major branch of a coronary artery (the anterior descending in these experiments) is associated with death of cardiac muscle if the occlusion lasts for 45 minutes or more. This is in accord with the studies of Blumgart[19] and co-workers and would vitiate the advantages of direct attack on the acutely obstructed artery from the standpoint of preventing muscle death, unless such an attack could be carried out during the "critical" period. Relief of a complete obstruction might still be beneficial in reducing the irritability of still viable but anoxic myocardium about the central area of necrosis.

Again, the problem of the partial obstruction and the emergency surgical efforts to relieve it and/or to prevent it from becoming complete is quite different and out of the scope of this paper.

CONCLUSION

A time study was undertaken to determine the period during which direct relief of a complete obstruction to a main branch of a coronary artery would prevent death of the portion of heart muscle supplied by the involved artery. The evidence presented indicates that a complete occlusion lasting for more than 45 minutes will produce the irreversible changes characteristic of myocardial infarction.

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OXYGEN CONSUMPTION DURING CARDIOPULMONARY BYPASS

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MUCH attention has been directed to studies of oxygen consumption during cardiopulmonary bypass, both in dogs and human beings. The difficulty of such studies is attested to by the variety of different results obtained by other investigators.

Attention is directed in the present study to the factors relating to oxygen consumption during extracorporeal circulation at varying perfusion rates in dogs and at flows of basal cardiac output in human beings.

METHODS

Part I. Dogs.—

Fifty-seven mongrel dogs were placed on total cardiopulmonary bypass with a gravity drainage rotating disc oxygenator for a minimum of one hour, under light Pentothal anesthesia, at varying flows. Oxygen consumption was measured in 25 animals by means of a Douglas bag just prior to thoracotomy. Operation was carried out via a right thoracotomy through the fourth interspace with cannulation of the superior vena cava, by way of the azygous vein, and inferior vena cava, by way of the right atrial appendage. The aorta was cannulated via the right carotid artery. The partial pressure of oxygen in the arterial blood was monitored by means of a Clark electrode polarographic circuit and was not allowed to rise above 200 mm. Hg. Arterial oxygen saturation was always over 90 per cent. Various intracardiac procedures were carried out, such as creation and closure of interatrial and interventricular septal defects which were not considered to interfere with metabolic studies.

Arterial and venous samples, drawn simultaneously during perfusion, were analyzed by the Van Slyke technique for oxygen content, oxygen capacity, and carbon dioxide content. Flows were measured following perfusion using the pump settings noted during perfusion and the same arterial catheter as used during perfusion. The validity of this method has been demonstrated by others and ourselves, when a completely occlusive pump is used.[1] The flow was kept constant for a minimum of 15 minutes prior to sample to ensure a steady state. One hundred and twenty observations were made on this group of 57 dogs. Oxygen consumption was calculated from the arterial-venous oxygen difference and flow. Rectal and blood temperatures were recorded for each oxygen determination and were always between 36° and 37° C. This was accomplished

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by means of a low spectrum infrared heater described in another publication The electrocardiogram and arterial and inferior vena cava pressures were monitored on a multichannel Sanborn recorder

Dog surface area was calculated by the following formula surface = 1.12 weight$^{2/3}$ (see Ref 2) Variations in arterial pressure venous oxygen saturation, and oxygen consumption were then related to flow in liters per square meter surface area per minute

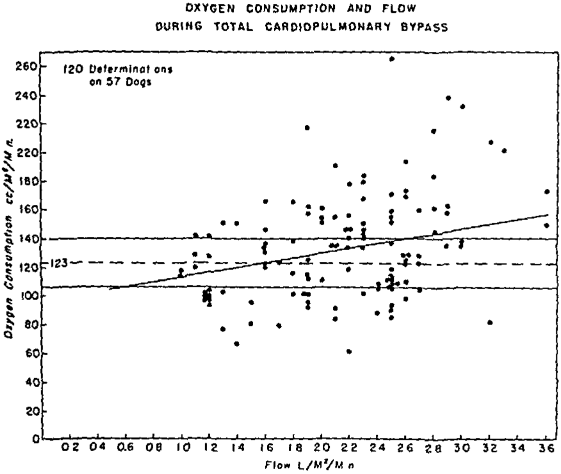

Fig 1—Relationship between oxygen consumption and flow described as a straight line function

$\hat{y} = 96.50 + 16.83\,x$

$s_{y \cdot x} = 28.74 \quad r^2 = 0.105$

t for slope $= 2.54 \quad P < 0.05$

The horizontal dotted line represents the mean oxygen consumption of 25 anesthetized dogs with the line above and below indicating two standard deviations

Part II Human Beings—

Similar data were obtained from the first 15 consecutive patients operated upon at the *University of Oregon Medical School Teaching Hospital* A flow approximating basal cardiac output was maintained constant throughout the perfusion period, utilizing the same apparatus as in the dog studies

An arterial sample was drawn from the patient 10 minutes prior to the onset of cardiac bypass At the 5 minute mark, following the onset of perfusion, and at 20 minute intervals thereafter, arterial and venous samples were drawn from the arterial end plate and venous reservoir, respectively An arterial sample was drawn 10 minutes following the cessation of cardiac bypass In addition to oxygen and carbon dioxide determinations using the Van Slyke method pH was measured with a Cambridge research model pH meter with a constant temperature air bath at 37° C and arterial buffer base calculated from the Singer Hastings normograms[3]

RESULTS

Part I. Dogs.—

As flow is increased in the entire range studied, oxygen consumption increases as demonstrated in Fig. 1. This rise in oxygen consumption continues as flow is increased above levels now in clinical use in many hospitals.

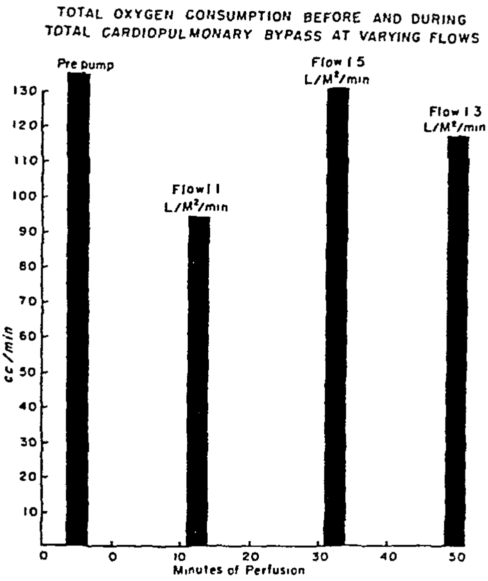

Fig. 2.

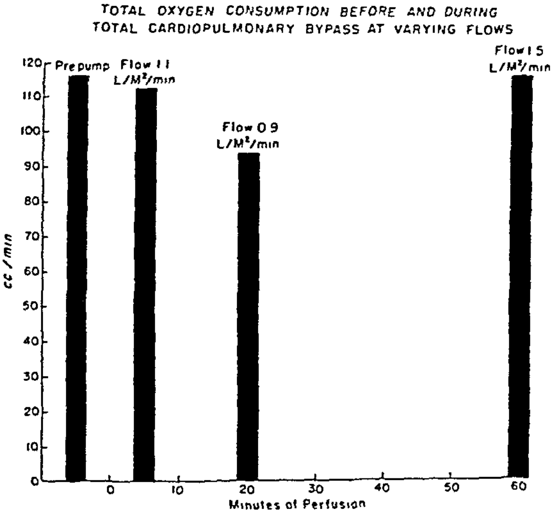

Fig. 3.

Figs. 2 and 3.—These figures demonstrate that changes in oxygen consumption will follow the same direction as changes in flow in a single animal.

The mean oxygen consumption prior to cardiac bypass but following tracheal intubation of 25 dogs in this laboratory is 123 c.c. per minute per square meter of body surface. When oxygen consumption during bypass is compared to this value, it is noted that at flows below 1.6 L per square meter of body surface there is greater tendency for oxygen consumption to be lower than the pre perfusion level and similarly, at flows above this value, there is greater tendency for the oxygen consumption to be higher than the pre perfusion value

As noted from Fig 1, there is great variation in oxygen consumption in different dogs at the same flow rate This is probably related to variations from the basal state, perhaps due to variations in the level of anesthesia All animals were similarly anesthetized with Pentothal sodium but it was noted that marked variations in the depth of anesthesia did occur and were difficult to avoid There is no doubt, however, that, whatever the effect of anesthesia higher flows will permit greater oxygen uptake by the experimental animal and this effect is a linear relationship in the range studied

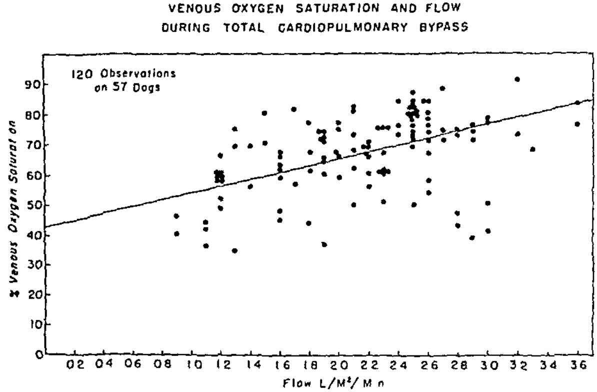

Fig 4—This figure demonstrates that venous oxygen saturation is well described by a linear function of flow and increases with increasing flow It is noteworthy that venous oxygen saturation of 70 per cent is obtained at a flow of 2.4 L/M /min

$\hat{y} = 42.85 + 11.33\ x$

$s_y \cdot x = 10.57 \quad r = 0.381$

t for slope $= 4.64 \quad P < 0.001$

The data in Fig 1 were compiled by describing 120 separate observations on 57 dogs It is of interest to document the effect of flow changes in a single animal This was done in Figs 2 and 3 where it is noted that changes in oxygen consumption will follow changes in flow regardless of the time relationship between high and low flows

Venous oxygen saturation increases in linear fashion as flow increases in the range studied as noted in Fig 4 In this large number of observations, although there is much scatter venous saturation is more likely to be 70 per cent or above at flows of 2.4 L per square meter of body surface or above

That the rise in oxygen consumption with increases in flow is not related to changes in perfusion pressure is demonstrated in Fig 5 in which there is no apparent relationship between flow and mean arterial perfusion pressure

TABLE I. MEAN PHYSIOLOGIC VALUES AND STANDARD DEVIATIONS IN 15 CONSECUTIVE PATIENTS UNDERGOING TOTAL CARDIOPULMONARY BYPASS*

Mean arterial pressure	73 mm./Hg ± 19
Mean venous pressure	11 mm./Hg ± 8
Arterial oxygen saturation	99% ± 6
Venous oxygen saturation	70% ± 7
Fall in pH*	-0.05 limits ± 0.1
Fall in buffer base*	-2.03 mEq. limits ± 3 mEq.
Partial pressure of carbon dioxide	35 mm./Hg ± 5
Oxygen consumption	133 c.c./M.^{2}/min. ± 36
Flow	2.735 L./M.^{2}/min. ± 0.4

*Patient described in Table V excluded.

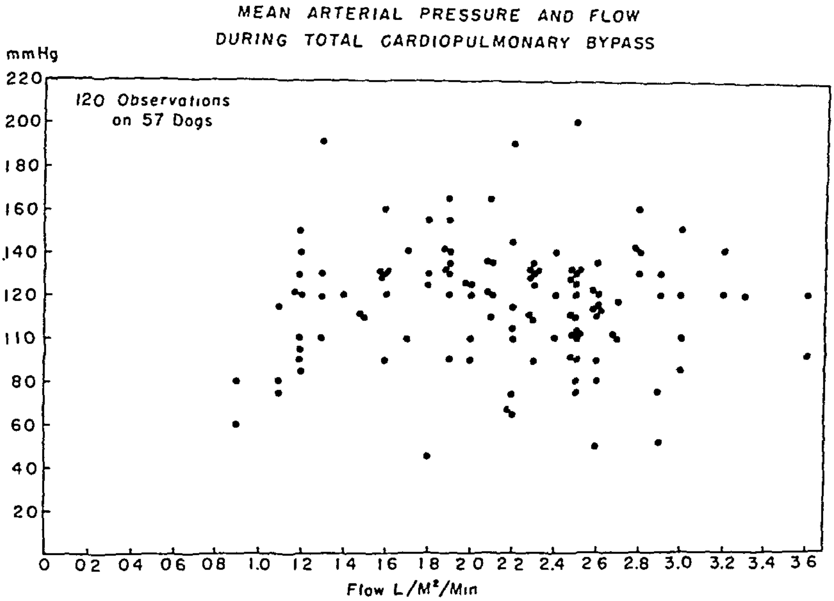

Fig. 5.—This figure demonstrates the lack of correlation between arterial pressure and flow during cardiopulmonary bypass in the dogs studied.

$\hat{y} = 125.15 - 4.32\ x.$

sy • x = 29.28, $r^2 = 0.011$.

t for slope = 0.79, $P > 0.25$.

Part II. Human Beings.—

In the fifteen consecutive human perfusions studied, the mean flow was 2.7 L. per square meter of body surface per minute with a range of 1.74 to 3.3. The mean values for mean arterial pressure, mean venous pressure, arterial saturation, venous saturation, fall in pH, fall in buffer base, and oxygen consumption are shown in Table I. The range of flows utilized in this series resulted in no essential deviation from the normal as seen by these mean values, except for 3 patients to be discussed in detail. In Table II, the venous saturations and oxygen consumptions at the 5-minute, 25-minute and 45-minute mark during perfusions are listed for each patient, along with the corresponding flow which was held constant throughout the entire perfusion period. The oxygen consumption is expressed as a percentage of the predicted basal oxygen consumption from the tables of Clark.[4]

TABLE II. VENOUS OXYGEN SATURATION AND OXYGEN CONSUMPTION RELATED TO BASAL PREDICTED OXYGEN CONSUMPTION DURING TOTAL CARDIOPULMONARY BYPASS AT HIGH FLOWS IN 15 CONSECUTIVE PATIENTS*

		5 MINUTES				25 MINUTES			45 MINUTES		
PATIENT	FLOW (L./M.²/MIN.)	VENOUS O_2 SAT. (%)	O_2 CONSUMPTION (C.C./M.²/MIN.)	PREDICTED O_2 CONSUMPTION (C.C./M.²/MIN.)	% PREDICTED O_2 CONSUMPTION	VENOUS O_2 SAT. (%)	O_2 CONSUMPTION (C.C./M.²/MIN.)	% PREDICTED O_2 CONSUMPTION	VENOUS O_2 SAT. (%)	O_2 CONSUMPTION (C.C./M.²/MIN.)	% PREDICTED O_2 CONSUMPTION
1	2.74	71	98	129	76	59	120	93	51	156	120
2	2.86	69	127	147	86	67	181	123	53	190	129
3	2.73	76	120	153	79	71	127	83	58	177	106
4	2.54	74	112	166	68	70	124	76			
5	3.05	68	121	144	84	66	154	107	61	177	122
6	3.52	75	90	162	56	69	153	95	74	185	114
7	2.78	77	106	152	69	79	101	66			
8	3.00	68	171	173	99						
9	2.58	72	129	163	78						
11	1.74	75	83	133	63	81	79	60	72	90	68
12	2.64	79	73	177	60	75	87	71	79	89	73
13	2.68	82	113	149	75	74	121	81			
14	2.47	72	96	174	50	63	156	90			
15	3.30	70	184	170	108	63	264	156			

*Patient described in Table V excluded.

It is of great interest that the oxygen consumption varied from 50 to 156 per cent of the predicted consumption from patient to patient, and also varied greatly in different samplings from the same patient, with a distinct tendency toward higher oxygen consumption in the latter periods of perfusion. Thus, of seven patients sampled at the 45-minute mark, 5 had oxygen consumptions over 100 per cent of the predicted value. Since the predicted value is based on observations in unanesthetized patients and it is known that anesthesia alone depresses oxygen consumption, the high values of oxygen consumption are surprising under the conditions of cardiopulmonary bypass. These findings would tend to invalidate a rigid method of calculating an optimal flow rate entirely on the basis of predicted basal oxygen consumption, or predicted basal cardiac output. The patient can have requirements well above basal levels under conditions of cardiopulmonary bypass.

Venous oxygen saturations below 70 per cent occurred only in those patients whose oxygen consumption was 86 per cent or above of the predicted basal consumption. However, in a small number of patients, perfused at 3 L. per square meter per minute or above, oxygen consumption above basal levels was supported during extracorporeal circulation with venous oxygen saturations of 70 per cent or more. This flow range, therefore, will maintain more normal findings in the venous saturation when oxygen consumption is above basal levels than will lower flows more closely approximating cardiac output under anesthesia.

Despite an attempt to avoid metabolic acidosis in all patients by utilizing high flows, there were three instances in this series of 15 patients in whom there was significant deviation from the normal values in pH and whole blood buffer base. The patient whose studies are shown in Table III had a low arterial saturation which was unsuspected during cardiac bypass because of a faulty cuvette oximeter. Despite what has been shown to be an adequate flow in the remainder of the series of patients, this patient developed mild metabolic acidosis.

TABLE III. THE EFFECT OF ARTERIAL UNSATURATION IN THE PRODUCTION OF MILD METABOLIC ACIDOSIS AT HIGH FLOWS

PATIENT NO. 1—FLOW 2.74 L./M.^{2}/MIN.
PREDICTED OXYGEN CONSUMPTION—129 C.C./M.^{2}/MIN.*

	Control	*5 min.*	*25 min.*	*45 min.*	*15 min. post-perfusion*
pH	7.37	7.34	7.30	7.26	7.21
Buffer base, mEq./L.	42	41	40	39	38
Partial pressure of carbon dioxide, mm. Hg	38	38	39	41	44
Arterial oxygen saturation	102%	96%	86%	81%	101%
Venous oxygen saturation		72%	59%	51%	
Oxygen consumption, c.c./M.^{2}/min.		99	121	157	
Per cent of predicted oxygen consumption		76	93	120	

*From tables of L. C. Clark.

The patient whose studies are shown in Table IV demonstrates that, when there is marked skeletal muscle activity during perfusion, what would ordinarily be an adequate rate will result in low venous oxygen saturations and mild metabolic acidosis. This patient was extremely light during perfusion with excessive motion of the diaphragm and extremities and a very high oxygen consumption. This, then, is a paradoxical situation in which a high oxygen consumption well above basal levels is associated with mild metabolic acidosis.

TABLE IV. THE EFFECT OF MUSCULAR EXERCISE IN THE PRODUCTION OF MILD METABOLIC ACIDOSIS AT HIGH FLOWS

PATIENT NO. 2—FLOW 2.86 L./M.²/MIN.
PREDICTED OXYGEN CONSUMPTION—147 C.C./M.²/MIN.*

	Control	*12 min.*	*26 min.*	*46 min.*	*22 min. post perfusion*
pH	7.46	7.34	7.31	7.26	7.37
Buffer base mEq./L.	42	42	40	40	40
Partial pressure of carbon dioxide, mm. Hg	31	37	39	44	31
Arterial oxygen saturation	104%	99%	98%	94%	95%
Venous oxygen saturation		69%	67%	54%	
Oxygen consumption c.c./M.²/min.		127	181	190	
Per cent of predicted oxygen consumption		86%	124%	129%	

*From tables of L. C. Clark.

The patient whose studies are shown in Table V suffered from primary pulmonary hypertension with no septal defect found at the time of ventriculotomy. Cardiac bypass could not be discontinued on this patient without resulting in acute heart failure, so that the patient was perfused for 8½ hours. A flow rate, which ordinarily would be adequate for the usual duration of perfusion, was demonstrated in this instance to be inadequate in preventing severe metabolic acidosis from occurring after many hours of cardiac bypass.

DISCUSSION

The relationship between flow and oxygen consumption during cardiopulmonary bypass is an important one. Paneth has stated that as flow is increased during total cardiopulmonary bypass in dogs with a bubble oxygenator from low levels to 1.2 L. per square meter of body surface per minute oxygen consumption increases and that a further increase in flow above this level does not result in a further increase in oxygen consumption. It is then inferred that flows above this level are unnecessary and perhaps undesirable since trauma to the blood in the extracorporeal circuit is roughly proportional to flow rate.[5]

Anderson and Senning,[6] on the other hand, have reported that increases in flow in the dog during cardiopulmonary bypass with the Crafoord-Senning pump oxygenator results in increasing oxygen consumption until flows above 100 c.c. per kilogram are obtained. At this flow, oxygen consumption during bypass approaches the pre-perfusion control level.

TABLE V. THE EFFECT OF A PROLONGED PERFUSION IN THE PRODUCTION OF MILD METABOLIC ACIDOSIS AT HIGH FLOWS

PATIENT NO. 10—FLOW 2.35 L./M.^{2}/MIN.
PREDICTED OXYGEN CONSUMPTION—169 C.C./M.^{2}/MIN.

	Control	*3 min.*	*23 min.*	*43 min.*	*1 hr.*	*1 hr. 23 min.*	*1 hr. 56 min.*	*2 hr. 18 min.*	*2 hr. 41 min.*	*3 hr. 44 min.*	*4 hr. 43 min.*	*5 hr. 43 min.*	*6 hr. 43 min.*	*7 hr. 43 min.*
pH	7.37	7.37	7.37	7.40	7.41	7.41	7.33	7.28	7.18	7.09	7.19	7.18	7.15	7.12
Buffer base	44	42	41	42	41	39	37	34	30	28	32	33	33	33
pCO_2	38	32	32	30	28	26	27	25	28	36	31	36	42	46
Venous oxygen saturation		67	68	74	63	78	77	77	72	64	70	60	67	49
Oxygen consumption		141	136	119	165	90	104	94	106	138	113	160	163	139
Per cent predicted O_2 consumption		83	80	70	98	53	61	56	64	82	67	94	97	82

The purpose of the present study was to obtain sufficient data on oxygen consumption in dogs, using the same apparatus and team as was planned for cardiopulmonary bypass in human beings and on the basis of these studies, to select the optimal flow range for initial clinical work. An attempt was made to achieve uniformity in all respects except flow rate. Oversaturation of the arterial blood was carefully avoided by the use of a Clark oxygen sensitive electrode. Disc speed was regulated to maintain a partial pressure of oxygen in the arterial blood between 100 and 200 mm Hg. The results of these laboratory experiments are not in agreement with those recorded by Dr Paneth and indicate that, at flows above 1.2 L per square meter of body surface per minute, oxygen consumption continues to rise, as flow was increased, in a linear fashion that is statistically significant. Oxygen availability and, hence, oxygen consumption appear to be depressed at flows significantly lower than normal cardiac output under conditions of anesthesia and normothermia. The reasons for the differences in experimental results are not immediately apparent but it is possible that the bubble oxygenator results in abnormally high pO_2 and, hence, because of a large amount of dissolved oxygen in the blood, flow requirements might be less than the requirement when the partial pressure of oxygen in blood leaving the oxygenator is carefully controlled and kept within the normal range.

As a result of these studies, it was elected to perfuse at flows approximating resting cardiac output in the first 15 consecutive clinical cases. The data obtained from these patients indicate the advantages of such a policy. Severe metabolic acidosis was not encountered, awakening from anesthesia was prompt, and all patients left the operating room in good condition except one who had primary pulmonary hypertension without a septal defect and could not be taken off the cardiac bypass. Oxygen consumption was quite high in almost all patients, with an average consumption approximating the basal oxygen consumption. In those patients with oxygen demands well above the predicted value, the high flow permitted an oxygen consumption above normal without undue widening of the arterial venous difference.

A surprising finding in one patient was that oxygen consumption above normal basal consumption may be inadequate in preventing mild metabolic acidosis when oxygen demands are excessive and pump output is limited to a flow of resting cardiac output. Under these circumstances, flow may be a limiting factor in oxygen consumption, and, hence, the perfusion defective in meeting body needs.

SUMMARY AND CONCLUSIONS

The relationship between flow and oxygen consumption has been studied in dogs and the flow range now considered adequate for human cardiopulmonary bypass. Oxygen consumption has been found to increase in a linear fashion as flow is increased in the range over 1.2 L per square meter of body surface per minute. Venous oxygen saturation increases in a linear fashion as flow is increased, and values of 70 per cent or more are more likely at flows of 2.4 L per square meter of body surface, or above, rather than at lower flows. Total body perfusion in human beings, at flows approximating basal cardiac output, will result in no tendency to metabolic acidosis except in three circumstances: (1) a low arterial saturation due to faulty oxygenator function, (2) excessive skeletal muscle activity during bypass, and (3) a prolonged perfusion. The concept of an ideal flow rate as one which is not in itself a limiting factor to oxygen consumption is put forward. This implies that the ideal flow will not bear a constant relationship to body weight or surface area but would be dependent upon oxygen needs as determined by body temperature, muscular activity, and perhaps other unknown factors.

The author gratefully acknowledges the technical assistance of Misses Mary Ellen O'Reilly and Patricia Starr, and Mr. Otto Hintz. The assistance and guidance of Drs. Donald Pitcairn and Herbert Griswold in conducting these studies were invaluable.

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PREVENTION OF SURGICAL HEART BLOCK BY THE USE OF SUPRAVITAL STAIN

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ONE of the serious complications of open heart surgery, using total cardio pulmonary bypass, is complete heart block resulting from direct surgical trauma to the cardiac conduction system Surgically induced atrioventricular dissociation occurs most frequently during repair of superiorly and posteriorly placed ventricular septal defects as well as in atrial septal defects of the ostium primum type In addition, patients with cyanotic congenital cardiac malformations and those with low cardiac reserve are prone to develop atrio ventricular dissociation under the stimulus of surgery alone, without actual trauma to the conduction system[1] Thus, while complete heart block can occur from other causes, direct surgical injury to the conduction system has now become the commonest form

The anatomy of the conduction system in relation to the right side of the heart is the key to the problem of surgical heart block[2] The atrio ventricular node lies immediately inferomedial to the mouth of the coronary sinus in the right atrium The bundle of His passes posterior to the annulus of the tricuspid valve and enters the right ventricle adjacent to the infero or superoposterior rim of the membranous ventricular septum The common bundle then divides into a right bundle branch which passes distally along the posterior margin of the membranous septum The left bundle branch pierces the ventricular septum and lies subendocardially immediately inferior to the aortic valve, where it then fans out along the left ventricular aspect of the septum Variations to this septal anatomic pattern occur chiefly in the presence of a ventricular septal defect of the membranous and posterior types If the common bundle passes distally along the posterior rim of a ventricular septal defect and divides into the right and left bundle at the *inferior* margin of the defect, there is a greater chance of developing complete surgical heart block than if the common bundle divides at the superoposterior margin of the ventricular septal defect and only the right bundle passes inferiorly along the posterior margin of the defect At present, during corrective cardiac surgery, there is no way of knowing which anatomic type is present

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We have been able to avoid surgical heart block by continuous monitoring of the electrocardiogram during the repair of ventricular septal or ostium primum defects. As dissociation changes in the electrocardiogram are observed, the surgeon is warned of his proximity to the conduction tissue. In this situation, by altering the suture placement, we have avoided complete and possibly fatal heart block on several occasions. However, if one induces potassium arrest, the heart is electrically inactive and the safeguard of a continuous electrocardiogram is lost. Indeed, some surgical centers have experienced an increased incidence of third degree heart block when cardioplegic agents have been used, the inference being that the bundle of His is more easily damaged when surgeons are unable to observe gross or electrical cardiac activity.[3]

To substitute for the loss of electrical activity in potassium arrest, we have attempted to visualize the conduction system by developing a supravital stain which (a) is transitory in action, (b) does not destroy the conduction tissue, and (c) is nontoxic in the general circulation.

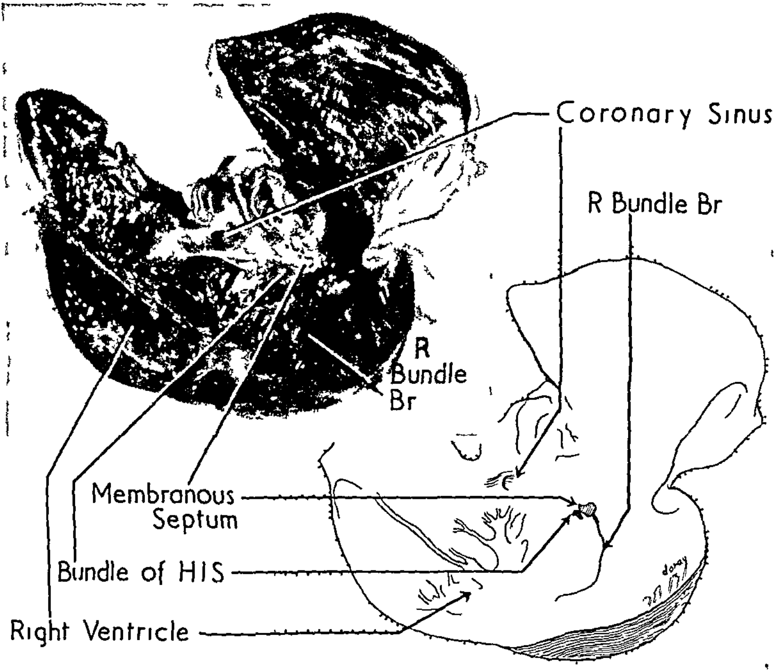
METHODS AND RESULTS

By trial and error a solution of elemental iodine was selected as the ideal supravital stain and tested in the hearts of dogs recently killed in other experiments. Five per cent elemental iodine dissolved in 10 per cent sodium iodide was the most satisfactory stain used to visualize the cardiac conduction tissue, clear visualization lasted 3 to 5 minutes before fading. Weaker solutions did not give a constant staining reaction and occasionally no staining occurred until the 5 per cent iodine solution was used. Stronger solutions, up to 10 per cent elemental iodine in 10 per cent sodium, gave more intense visualization for longer periods which were considered unnecessary. Due to the depressing effect of potassium on cardiac function, sodium (Na I) was used as the vehicle for dissolving the 5 per cent elemental iodine.

Staining reactions were repeated in the hearts of live dogs. Eight mongrel dogs were given a Pentothal Anectine anesthetic and placed on the bubble oxygenator with total cardiopulmonary bypass, following which potassium arrest was instituted using the Melrose technique.[4] The right ventricle was opened and the conduction tissue stained with varying solutions of elemental iodine in 10 per cent sodium iodide. The intensity and duration of the staining reaction was recorded. Potassium arrest was terminated after 10 minutes and, following return of sinus rhythm, the pump-oxygenator was discontinued.

In 7 of the 8 dogs, good staining visualization of the bundle of His and, particularly, the right bundle branch was obtained (Fig. 1). Of the seven successfully stained hearts, six were quickly restored to sinus rhythm at the completion of 10 minutes of induced cardiac arrest, while one dog developed uncontrolled ventricular fibrillation as the result of faulty perfusion technique. In one dog, the bundle failed to stain due to the constant wash of blood across the endocardium from several sources uncontrolled by suction The endocardium overlying the conduction tissue must be dry before staining can occur, indeed, blood from any source will prevent visualization of the common bundle or its branches by the iodine method

In the 8 dogs staining was commenced with 0 5 per cent elemental iodine followed by 1 per cent, 2 per cent, 4 per cent and 5 per cent solutions The 0 5 per cent to 4 per cent solutions gave inconstant visual reactions but 5 per cent solutions stained clearly for several minutes before fading In a series of 4 dogs 10 per cent iodine solution stained the conduction tissue intensely for 7 to 15 minutes which was longer than necessary Although sinus rhythm was restored in the 4 cases the period of resuscitation, after 10 minutes of potassium arrest, was distinctly prolonged and more difficult when compared to the cases using 5 per cent iodine It is suggested that the more intense staining reactions (10 per cent) are dangerous and can produce permanent damage to the conduction system



U B C Dept of MEDICAL ILLUSTRATION

Fig 1

General toxicity of the 5 per cent elemental iodine solution was tested by slowly injecting 3 to 5 c.c. into the pulmonary artery of 4 dogs, all of which recovered completely and without incident. Since the amount of 5 per cent iodine solution used for staining is only 1 c.c. there appears to be a wide margin of safety.

Fixed sections of dog myocardium containing the right bundle branch were stained with periodic acid-Schiff (PAS). The muscle and conduction tissue contained pink staining cytoplasm that was attributed to glycogen. To prove this, sections were first immersed in diastase before PAS staining, and no pink cytoplasm was seen in any tissue. Next, histologic sections of myocardium containing the right bundle branch were immersed for periods up to 72 hours in 5 per cent iodine solution in 10 per cent sodium iodide and then stained with PAS. Microscopically, these sections all showed the same amount of pink staining glycogen in the conduction tissue as did the control sections stained only with PAS but not immersed in iodine.

This would suggest that the iodine stain, while combining with glycogen of cardiac conduction tissue, does not destroy it, nor produce irreversible changes during the short periods of contact at surgery.

DISCUSSION

In the last three years, great advances have been made in the treatment of surgically induced heart block. Initially, intravenous and rectal Isuprel* were used to increase ventricular rate and maintain a satisfactory cardiac output in the presence of complete atrioventricular dissociation. Some patients, however, become refractory to Isuprel[1] and develop ventricular bradycardia with poor coronary artery filling and fatal cardiac arrest. The brilliant development by the Minnesota group of a myocardial wire and mechanical cardiac pacemaker has successfully treated many patients with severe surgical third degree heart block.[5]

Our purpose has been to develop a method of *preventing* surgical heart block by visualizing the bundle of His and, during the short period of supravital staining, to effect safely the placement of closing sutures in the ventricular septal or ostium primum defects. We have used the staining technique on 3 patients. The first was a 9-year-old boy with a common ventricle that was repaired by making an Ivalon septum. It was difficult to determine the exact site of suture placement since no remnant of septal tissue was present. After potassium arrest was instituted, 5 per cent elemental iodine in 10 per cent sodium iodide solution was painted on the endocardium of the common ventricle to show a lacy conduction network on the supero-anterior and superoposterior aspects. In this way, sutures were placed in the wall where conduction tissue was absent, and upon completion of the repair the potassium arrest was terminated with rapid restoration of sinus rhythm.

The second patient was a 3-year-old boy with advanced pulmonary hypertension and a large ventricular septal defect. Following potassium arrest it was possible to see that the defect involved the entire septum from the crista supraventricularis distally to the pulmonary and aortic valves which were separated by a millimeter of fibrous tissue Five per cent iodine solution outlined either the common bundle or the right bundle branch in the postero-inferior margin of the septal defect and, as a consequence, sutures were placed wide of this tissue in effecting a repair After completion of arrest, sinus rhythm was restored

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*Available from Winthrop Laboratories, New York, N. Y.

The third case involved an 8-year-old girl with a membranous ventricular septal defect and a pulmonary artery pressure of 90/40 mm Hg Following induced potassium arrest, 5 per cent iodine solution was painted along the margins of the defect but failed to show conduction tissue Following repair of the defect, the patient developed permanent third degree heart block It is probable the conduction bundle failed to stain because it was deep within the ventricular septum and beyond the penetration of the iodine solution

This is a preliminary report, based on experimental work and limited patient application However, we believe that, with further experience, supravital staining of the conduction system in the right ventricle will add to the safety of potassium arrest and may reduce the incidence of complete heart block in the electrically inactive myocardium

SUMMARY

The desirability of transitory visualization of the bundle of His in the potassium arrested heart is discussed

Five per cent elemental iodine in 10 per cent sodium iodide was the most satisfactory supravital stain used to outline the cardiac conduction system of the right ventricle

Experimental work and brief patient experience is outlined

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ACUTE PERICARDIAL FAT NECROSIS

Report of a Case

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THE PERICARDIAL fat necrosis syndrome was first recognized as a clinicopathologic entity by Jackson, Clagett, and McDonald.[1] The authors enphasized the fact that this lesion can simulate the symptomatology and physical findings of acute myocardial infarction, pulmonary embolus, or hemorrhage into a neoplasm of the lung. The roentgenographic appearance may easily be misinterpreted as a primary or metastatic carcinoma of the lung, a localized pleural effusion, pleuropericardial cyst, or mesothelioma. A consideration of this disease entity is, therefore, warranted in any patient with unexplained precordial pain, pleuritic pain in the left lower chest, and an associated juxtacardiac mass.

Jackson, Clagett, and McDonald[1] reported 3 cases of pericardial fat necrosis in which exploratory thoracotomy was performed from 7 to 10 weeks after the acute onset of symptoms. In the following case of pericardial fat necrosis, an exploratory operation was made 13 days after the acute onset of symptoms. This case afforded us an opportunity to observe and describe the pathologic changes of the acute phase of this recently recognized clinical syndrome. To the best of our knowledge a description of the early stage of this lesion has not appeared in the literature.

CASE REPORT

The patient was a 46-year-old white male carpenter. On Feb. 4, 1958, he was treated for an upper respiratory infection. He had fever, nonproductive cough, generalized aching, and fatigue. A chest roentgenogram was found to be within normal limits (Fig. 1, *A*). The patient recovered within a few days with antibiotic therapy.

On Feb. 14, 1958, the patient experienced the sudden onset of left lower anterior chest pain and cramping epigastric pain. The onset of this pain occurred during a severe lifting effort, when it is estimated that he exerted a lifting force equal to 150 to 200 pounds. This pain radiated to the left shoulder and increased in severity on deep inspiration. The pain, subsequently, became excruciating and caused a brief episode of syncope. He was hospitalized on Feb. 17, 1958, with an admitting diagnosis of acute myocardial infarction. His past medical history revealed that there were recurrent duodenal ulcer symptoms and one episode of bleeding during the past 18 years. However, the patient had been free of ulcer symptoms during the past year.

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Physical examination on admission to the hospital revealed a white man, 5 feet 11 inches tall, weighing 157 pounds. He was pale, sweating, and in excruciating chest pain. Respirations were rapid and shallow, blood pressure 98/68 mm. Hg, and pulse 126. He was unable to take a deep breath because of the exacerbation of the chest pain. Auscultation of the chest elicited normal breath sounds and fremitus in the lung fields. An unusual, soft, low-pitched rub was heard during expiration, synchronous with systole at the cardiac apex. This sound closely resembled the sound produced by compressing a wet sponge. It could easily be distinguished from the classical friction rub of a pericarditis. The rub disappeared on the third hospital day.

Although there was moderate improvement of the pain with the administration of Demerol and oxygen, the patient remained in a state of shock. With the administration of Levophed by intravenous drip, his general condition finally improved. Within several hours his blood pressure stabilized to 126/82 mm. Hg, and the Levophed was discontinued.

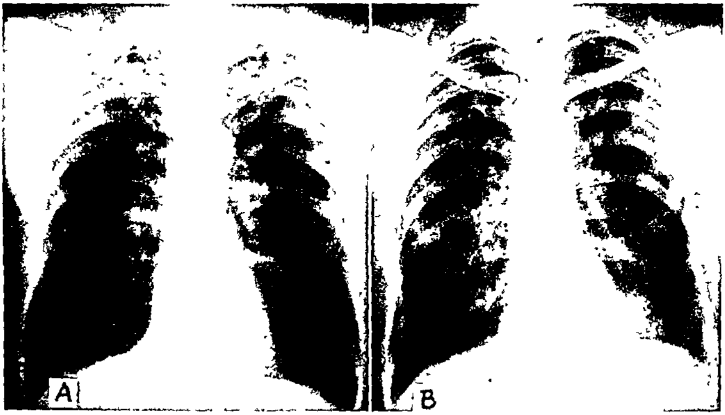


Fig 1—*A*, Roentgenogram taken 10 days prior to the onset of symptoms.
B, Roentgenogram taken 3 days after the onset of symptoms Note the appearance of a juxtacardiac mass represented by the area of increased density along the left border of the cardiac shadow.

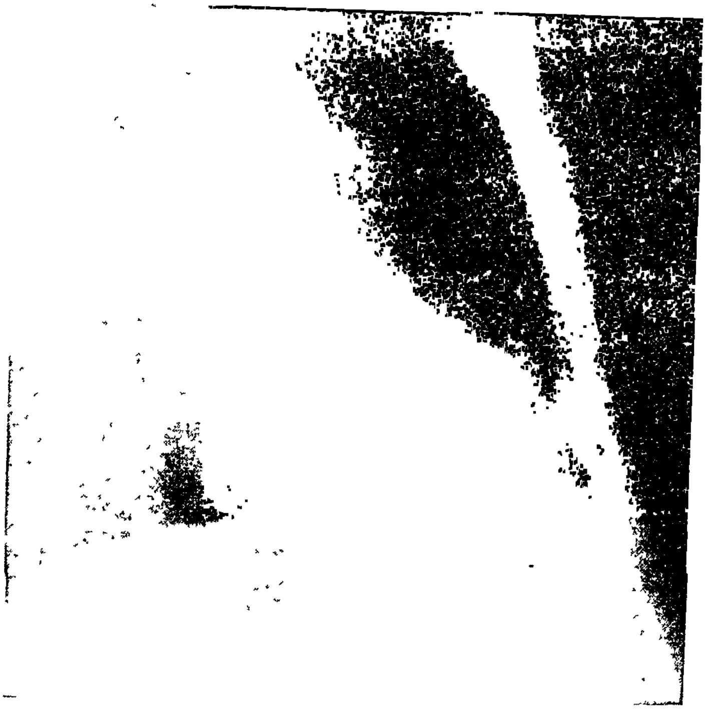
An electrocardiogram was normal, except for an occasional ventricular presystole. The corrected sedimentation rate was 12 mm. Chest roentgenograms (Figs. 1, *B* and 2) demonstrated a juxtacardiac mass along the anterior aspect of the left cardiac border.

Serial electrocardiograms and serum transaminase determinations were normal. Tomograms of the juxtacardiac mass revealed several ovoid areas of decreased density (Fig. 3).

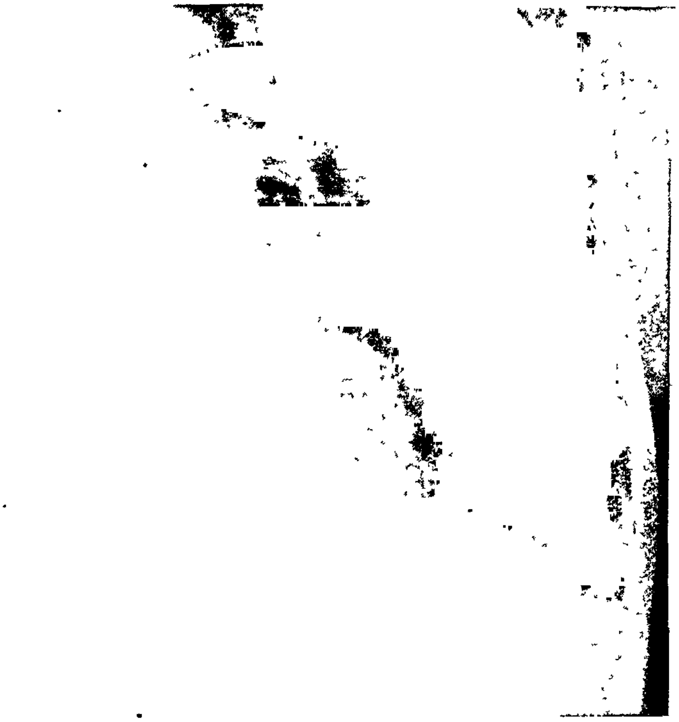
During the following week the patient's general condition improved considerably, although the left chest pain persisted in severity.

On Feb 27, 1958, an exploratory operation was performed through a left anterolateral incision in the sixth intercostal space. A firm ovoid mass, measuring 10 by 7 cm., was identified as the pericardial fat pad. It was adherent to the anterior and lateral aspect of the pericardium and the anterior chest wall. There were also adhesions binding the lingula to the pericardial fat pad The mass was excised by blunt dissection from the pericardium, anterior chest wall attachments, and lingula

Grossly, the specimen measured 10 by 7.5 by 3.0 cm. (Fig. 4). It consisted of fatty tissue. The external surface was focally indurated and varied from a mottled light brown to a red-black hemorrhagic discoloration. A sharply delineated hemorrhagic area at the



g. 2.—Lateral view demonstrating an ovoid density due to the enlarged pericardial fat pad.



. 3.—Tomographic section study demonstrating saccular radiolucent areas within the pericardial fat pad.

superior end (Fig. 4) measured 2.2 cm. Other areas of subcapsular extravasation of blood were noted. The cut surface a few centimeters from the hemorrhagic area appeared to be homogenous and had a normal fatty color.

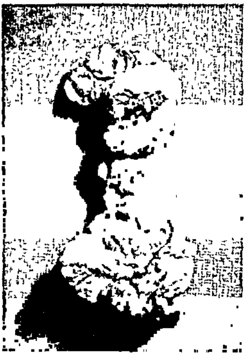


Fig. 4.—Gross specimen of resected pericardial fat. The dark areas contained old blood. The specimen measured 10 by 7.5 by 3.0 cm

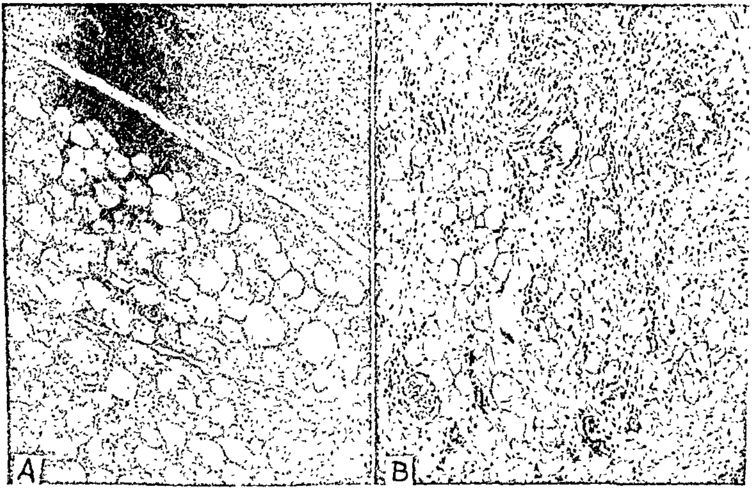


Fig. 5.—*A*, Section of tissue in area of hemorrhagic necrosis showing extravasation of blood and infiltration of inflammatory cells.

B, Section of tissue from the periphery of area of hemorrhagic necrosis showing fibrosis and chronic inflammatory cells.

Histologically, the tissue revealed acute hemorrhagic infarction with considerable interstitial hemorrhage, necrosis of blood vessels, and sparse infiltration with polymorphonuclear leukocytes and lymphocytes (Fig. 5, *A*).

At the periphery of the infarcted areas, lipophagic cells were seen and there was a zone of ulcerous granulation tissue infiltrated with acute and chronic inflammatory cells.

this tissue, occasional arterioles were seen the walls of which were infiltrated by polymorphonuclear leukocytes (Fig. 5, *B*). These cells spilled over into the perivascular spaces. A few arterioles showed subintimal fibrous thickening of a moderate degree. Bacteria or fungi were not demonstrable.

COMMENT

The clinical characteristics of this disease, as observed in our patient, were similar to those found in the 3 cases reported by Jackson, Clagett, and McDonald. However, there were several exceptions. This patient was not obese; to the contrary, he was thin and tall. This fact denies the concept that the lesion occurs only in the obese. In addition, there was a temporal and probably a causative relationship between the severe lifting effort and the acute onset of symptoms. The strain of this lifting effort produced the hemodynamic changes and stresses of a Valsalva maneuver. There is strong probability that a traumatic etiology was present in our case. The presence of neurogenic shock and cardiac arrythmia, which were concomitant findings in the early period of hospitalization, caused us to assume that we were treating a case of myocardial infarction with early coronary shock.

Although the pathogenesis of this lesion is still obscure, it is possible that its onset is primarily a "vascular accident" with the resultant extravasation of blood from an artery, hematoma formation and thrombosis. Consequently, the blood supply to the fatty tissue is compromised with the resultant ischemic fatty necrosis.

A comparison of the acute and chronic phases of pericardial fat necrosis would lead one to assume that there is absorption of the extravasated blood, subsequent fibrosis, and ischemic necrosis of fat. This assumption would seem to be justified by observation of the changes in the pericardial fat specimen. The transition from acute hemorrhage to organization, fibrosis, ischemic fat necrosis, and endarteritic changes is clearly demonstrated.

SUMMARY

1. A case of acute pericardial fat necrosis treated by surgery 13 days after the acute onset of symptoms is presented.

2. The symptoms of acute onset of precordial pain, pleuritic pain in the left chest radiating to the left shoulder, and the demonstration of a juxtacardiac mass in the thoracic roentgenogram are the principal findings in this syndrome. A precordial systolic rub also may be heard.

3. Tomographic section studies may show radiolucent ovoid areas which probably represent normal fat lobules surrounded by hemorrhagic, necrotic, and fibrotic tissue.

4. Histologically, the changes were due to extravasation of blood, ischemic fat necrosis, and fibrosis. Moderate endarteritic changes were also noted.

5. The traumatic etiology is a strong probability in our case.

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MYOCARDIAL REVASCULARIZATION THROUGH A GASTRIC PEDICLE

An Experimental Study

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A NUMBER of methods have been and are being used clinically to improve the blood flow to the myocardium in cases of coronary artery disease, and some surgeons are advocating that procedures be done on an almost routine basis as patients approach middle age. The diversity of the methods advocated and the lack of any clear cut proof that benefit will result put the present clinical work on an uncertain basis. Because of the inherent difficulties of clinical evaluation of coronary disease, compelling proof must be forthcoming from animal experimentation before surgical correction of coronary disease will be a generally accepted procedure. The more promising experimental methods, at present, make use of pedicle flaps of skin or alimentary tract.[1-10] That such a pedicle flap can carry useful blood to a parenchymal organ has been clearly demonstrated for the kidney.[6] Other procedures are generally theoretically less sound or are too difficult technically. It is likely that intelligent use of pedicle flaps will result in real improvement in coronary artery disease, providing simple production of extracardiac anastomoses will, in fact, lead to greater myocardial blood supply. This preliminary report concerns the formation of an adequate pedicle flap from the stomach and a method for evaluating its efficacy by direct measurement of the myocardial oxygen tension. The stomach was chosen because of its ready accessibility from the chest, its close proximity to the heart, its rich blood supply, and the relative ease of performing plastic surgery on this organ. This method of study was chosen because more usual methods concerned with mortality, or the anatomic demonstration of communications have not yielded clear cut results.[4, 10]

MATERIALS AND METHODS

Mongrel dogs are operated on in a standard manner through the left eighth interspace. A portion of the stomach is delivered through an incision in the ligamentous portion of the diaphragm (Fig. 1). A flap about 2½ inches on a side, based on the superior portion of the lesser curvature, is raised on the anterior aspect of the stomach, much as is done in performing a Janeway gastrostomy (Fig. 2). The mucosa is removed from this flap, the stomach is closed in a

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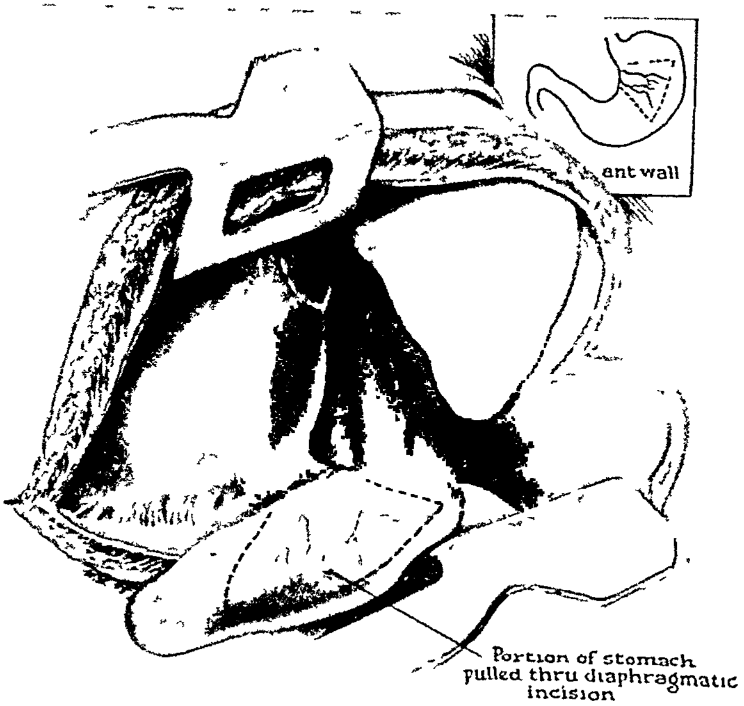
Fig 1.



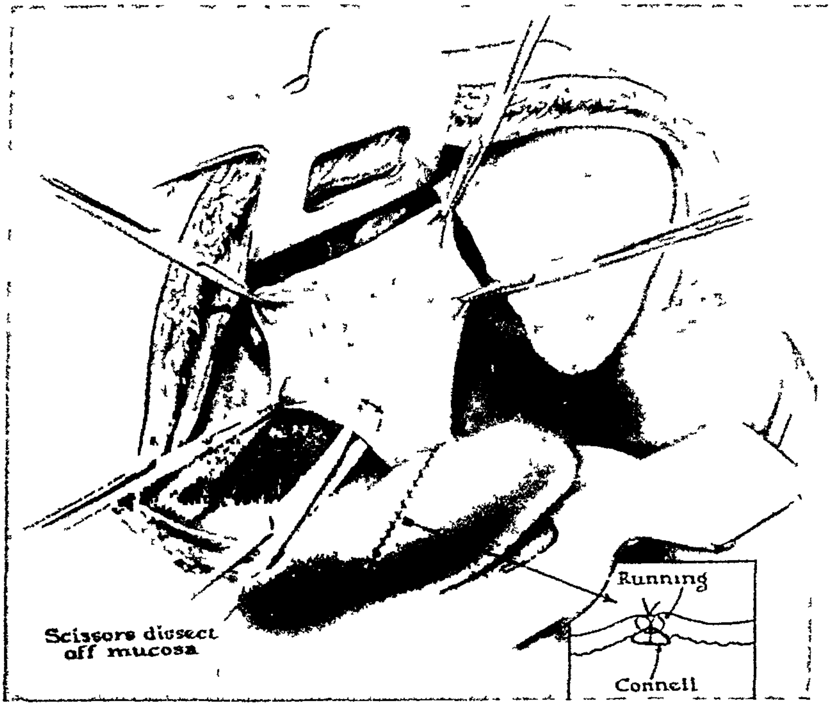
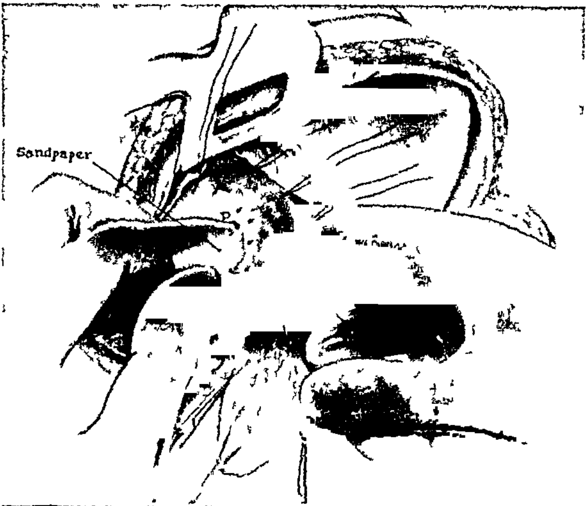


Fig 2

Fig 1.—The stomach is readily accessible through the diaphragm adjacent to the apex of the heart

Fig 2.—The plastic flap based on the lesser curvature is freed of mucosa and the stomach is then closed in a routine manner

Fig 3



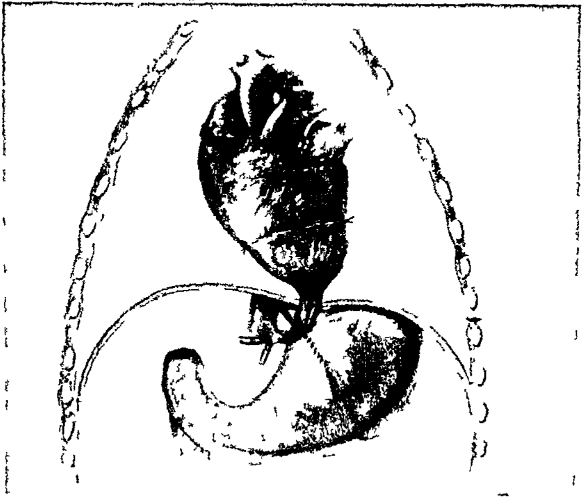


Fig 4

Fig 3—After the apex of the heart has been abraded with sandpaper the prepared flap is sutured to the heart with fine silk The position of the sutures is shown in the figure

Fig 4—The general relationships of the cardiac apex the pedicle flap the lesser curvature of the stomach and the blood supply via the left gastric artery are shown

routine manner, and the diaphragm is closed about the base of the pedicle. A long pericardial incision is made parallel to the phrenic nerve, and the apex of the heart is delivered and abraded lightly with fine "wet-dry" sandpaper (Fig. 3). The raw surface of the pedicle flap is then attached to the myocardium by interrupted sutures of 4-0 silk. As applied, the flap generally measures 8 to 10 cm. in diameter and covers portions of all the major coronary arteries. Closure of the pericardium provides firm pressure to approximate the flap to the myocardium. The chest is then closed in a standard manner, without drainage. The relationship of the completed pedicle to the heart, diaphragm, and stomach is seen in Figs. 4 and 5. The procedure is generally carried out without blood replacement and the animals present no special postoperative problems.

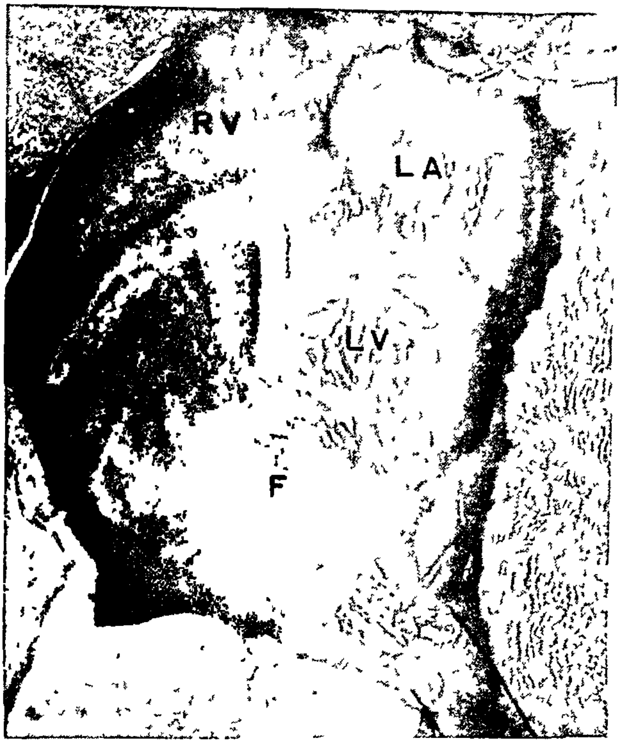


Fig 5—A completed pedicle flap at approximately 6 weeks There is relatively little pericarditis The flap is firmly attached to the heart *RV*—right ventricle, *LV*—left ventricle; *LA*—left atrial appendage, and *F*—pedicle flap A ligature has been loosely placed about the pedicle of the flap preliminary to occluding its blood supply

The second thoracotomy for study is generally done 6 to 8 weeks later. Surviving animals are sacrificed. Postmortem arterial injections are done in a few animals and, in most instances, routine histologic preparations are made

Oxygen studies, mainly of the left ventricular myocardium, have been carried out in control dogs, dogs with pedicles, and dogs with pedicles in whom previous ligation of the anterior descending coronary artery had been done Ligation of the anterior descending coronary has always been performed at its take-off from the left coronary artery. The platinum microelectrode as described by Davies and Brink[8] and by Montgomery and Horowitz[9] has been used for these studies. A special electrode developed by George Peirce at the University of Pennsylvania has proved useful for myocardial measurements (Fig. 6).[11] In practice, the platinum microelectrode transmits a current, which can be read on a sensitive galvanometer, that is directly proportional to the oxygen available to it, when 0 6 volt driving force is delivered to the electrode This appears to be based on the fact that the current is transmitted by the electrolysis of oxygen and, even in complicated solutions, this reaction accounts for the entire flow of current The electrodes give only relative readings but are sufficiently stable for acute experiments The changes in oxygen tension are of great magnitude

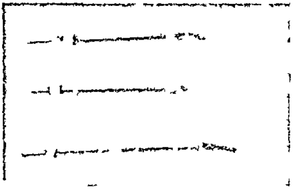


Fig 6 —Three platinum microelectrodes are shown in approximately natural size Platinum wire is sealed in glass and the tip is sharpened The illustrated electrodes have tips of varying length shown distal to the white bead A drop of mercury in the tiny polyethylene tube is used to make contact with the lead wire

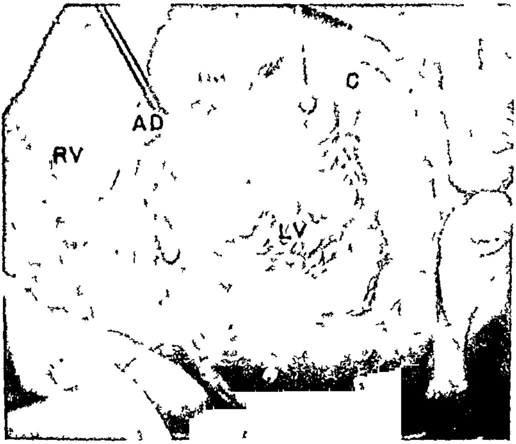


Fig 7 —Five electrodes are shown in place in a normal beating heart They can be located where desired in relationship to the various coronary arteries In animals with a pedicle flap usually at least one electrode is placed in the flap itself *RV*—right ventricle *LV*—left ventricle *AD*—anterior descending coronary artery *C*—circumflex coronary artery A ligature has been placed about the origin of the anterior descending artery preparatory to ligation

Multiple electrodes may be used and they may be read continuously or intermittently For simplicity, five electrodes appropriately spaced are used and each electrode is read at one minute intervals In general, some electrodes are placed in the area which would be expected to become ischemic on anterior descending coronary ligation, some are placed in the area supplied by the circumflex artery, and generally one is placed in the flap itself (Fig 7)

RESULTS

There have been only three deaths in twenty-five preparations. It is necessary to remove the mucosa meticulously because, in 2 dogs, mucosa-lined pockets developed between the flap and the surface of the heart. All of the other dogs had firmly adherent pedicles and were satisfactory for study. The presence of vessels crossing between pedicle and myocardium was demonstrated in the injection preparations and vessels of arteriolar size were frequently seen in routine sections.

Although the number of experiments is much too small to justfy any conclusions, some very provocative data have been obtained. The myocardial electrodes are relatively less sensitive to the dog's breathing 100 per cent oxygen than are similar electrodes placed in the skin. A change from air to oxygen increases the arterial oxygen tension about fivefold and, in the skin, increases of from 300 to 700 per cent in readings are quite usual. In the heart, increases of 50 to 200 per cent are more often the rule (Fig. 8). Electrodes placed beyond the zone of ischemia produced by coronary artery ligation show relatively constant readings. Electrodes in the zone of ischemia show an extremely rapid drop, essentially to zero. In control dogs, these low readings continue for a matter of minutes until the dog dies of ventricular fibrillation, which has occurred in every instance. In some dogs with flaps, the electrode readings follow this same pattern, but in some there is a gradual, although modest, climb indicating an increase in the oxygen tension in the ischemic area. Subsequent ligation of the pedicle in these dogs again reduces the readings nearly to zero. These studies appear to demonstrate a definite flow of blood through the flap to the heart in at least some of the animal preparations.

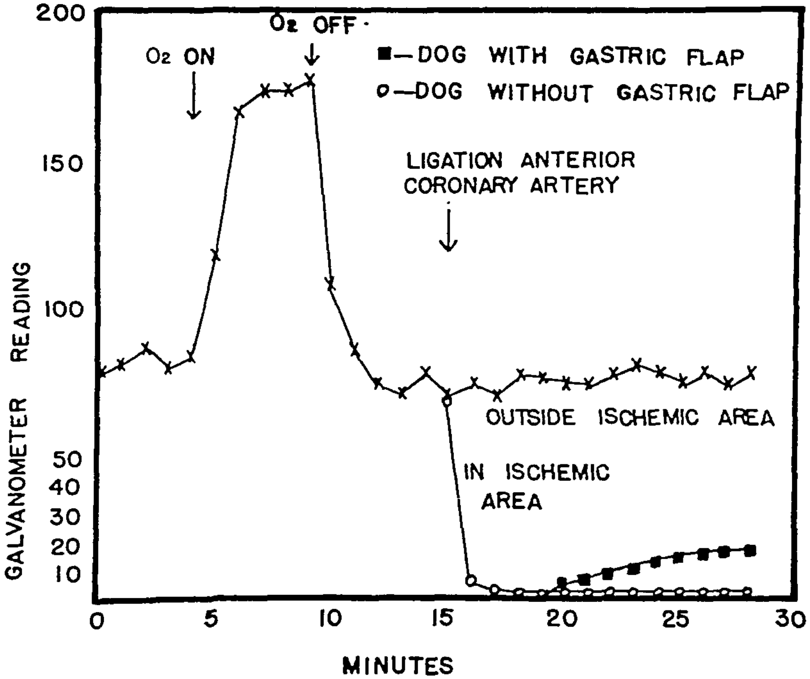


Fig. 8.—Galvanometer readings of several myocardial electrodes have been averaged. The pattern illustrated does not always occur. For explanation of figure see text.

A frequent problem has been the sudden onset of ventricular fibrillation, which has terminated many experiments prematurely. This difficulty has not yet been solved.

DISCUSSION

Clinical evaluation of coronary artery disease is extremely difficult, because of the almost constant psychic overlay in patients and the subjective nature of the symptoms. Objective evaluation by exercise tolerance or by reversion of the electrocardiogram toward normal is not satisfactory since in the first place there is a tendency for angina to improve spontaneously and in the second place, a revascularization procedure may itself produce abnormal electrocardiographic changes.

The problem is complicated in dogs because of the ease with which blood flow to an individual area of the heart may be increased by development of intrinsic intracoronary anastomoses.[4, 6, 1] In the first place any procedure including a sham operation on the heart, will apparently protect a dog to a certain extent from myocardial ischemia following ligation of a coronary artery.[8] The only satisfactory explanation for this is development of a collateral circulation within the heart. In the second place, one cannot produce a preparation with chronic coronary insufficiency by coronary artery ligation.[1] Dogs with all three main coronary trunks ligated in stages may be able to run normally on a treadmill.[3]

It would appear then that the experimental results must be viewed circumspectly. Improvement in mortality in a given experimental preparation following coronary artery ligation, even if statistically valid, does not indicate that the procedure increases the extrinsic blood supply of the heart. It may reflect simply an increase in the effective anastomoses between the existing myocardial vessels. In like manner, the demonstration of vessels passing between the pedicle and the heart anatomically does not indicate the direction or the magnitude of blood flow. The coronary backflow method advocated by Beck, gives some indirect information regarding the status of both intra- and extracoronary anastomoses. It can be shown, for instance, that, early after a coronary sinus anastomosis, back bleeding from the cut circumflex artery is increased and that the increase is less if the coronary sinus anastomosis is clamped.[6] Since the procedure involves reversing the blood flow and decreasing the pressure in the bed of the circumflex artery it is not physiologic and interpretation of the data is hazardous.

Measurement of myocardial oxygen tension records objectively and graphically by means of an important physiologic variable what is quite obvious visually following major coronary artery ligation, the appearance of an area of ischemia marked by cyanosis and sometimes by paradoxical motion. Except for the necessity of leaving the chest open, the method is a physiologic one. Changes in potential blood supply resulting from the experimental flap can be elucidated by measuring the oxygen tension change when the flap is clamped. It should be possible with this method to determine if there is a useful increase in extracoronary blood flow from the gastric flap in the present preparation or, for that matter, if a variety of other preparations increase extracardiac flow

In this regard, it seems particularly unfortunate that methods of treating myocardial insufficiency by procedures such as internal mammary ligation, which defy evaluation, should be used clinically.

Since experiments are frequently interrupted by ventricular fibrillation, it is planned to modify the experimental procedures a little to decrease the incidence of this arrhythmia and permit oxygen tension data to be obtained over longer periods of time. Contemplated modifications include: (1) slow coronary occlusion with Berman "buttons,"[2] followed by oxygen tension studies on ligation of the pedicle, (2) surgical implantation of microelectrodes, so that studies can be done in closed chest preparations, and (3) ligation of smaller branches than the anterior descending coronary artery to decrease the incidence of ventricular fibrillation.

SUMMARY

A satisfactory method of fashioning a vascular pedicle from the stomach and anastomosing it to the apex of the heart is described. The evaluation of blood flow in the pedicle by measurement of myocardial oxygen tension is discussed. No conclusions are drawn concerning the efficacy of the experimental procedure in increasing the myocardial blood supply in this preliminary report. Plans for improved experimental methods are given.

ADDENDUM

One patient has had the described operation for intractable angina pectoris. Technically, the operation was entirely satisfactory and there were no digestive or diaphragmatic problems postoperatively.

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FORWARD VERSUS RETROGRADE CORONARY PERFUSION FOR DIRECT VISION SURGERY OF ACQUIRED AORTIC VALVULAR DISEASE

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THE aortic valve is the most impregnable orifice of the human body. It may well be the last anatomic frontier of surgery. Its diseases are among the most difficult cardiac lesions to treat. Moreover, the risk of attempting to modify the pathologic architecture of the aortic valve often assumes dimensions all out of proportion to the amount of relief usually derived from a "successful" procedure. Many heart surgeons refuse to deal with any deformity of the aortic valve, and most are skeptical of the efficacy of surgery in calcific acquired disease and congenital stenosis without poststenotic dilatation. Until the mortality now associated with excursions in front of the aortic valve is substantially decreased, pleas for early operation are likely to continue unheard by cardiologists. This report will deal primarily with experimental efforts to provide a smoother avenue to the aortic tunnel.

Human application of Alexis Carrel's experimental work on the aortic and pulmonary valves, reported in 1910[1] and 1914[2], came slowly and at great cost. Blind approaches, initiated by Tuffier,[3] Brock,[4] Smithy and Parker,[5] and Niedner[6] and popularized by Bailey[7] and Glover[8] and their associates, are clearly inferior to any direct method the performance of which is attended by a respectable operative risk. After the work of Neville and Clowes[9] exposed Cookson's[10] misconception that the sucking action of the beating heart would predispose to coronary air embolism, Lewis,[11] Swan,[12] and Lillehei[13] operated upon the aortic valve under direct vision. The open method achieved introduction if not approbation.

In the 3-year period since the inauguration of direct vision surgery for the aortic valve, certain improvements and changes have developed. The always hurried, often frantic, valvulotomy, during hypothermia alone, is obsolete. Lewis[14] prefers the membrane oxygenator and moderate hypothermia with coronary perfusion; this permits unhurried, calculated surgery of the aortic valve. In most cases, Lillehei[15] feels that the bubble oxygenator with some kind of coronary perfusion at normal temperature is the *least difficult technique.*

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It seems at this writing that congenital aortic stenosis differs importantly from acquired disease in that an oxygen source is not essential for the myocardium during valvuloplasty. Depleted cardiac reserve, usually present in acquired lesions, necessitates the use of some kind of coronary perfusion. Elective cardiac arrest with potassium citrate, acetylcholine, ventricular fibrillation, or anoxia is probably not advisable in most cases of acquired aortic disease.

The experiments reported herein pertain to the delineation of improved methods for coronary perfusion during exposure of the aortic orifice. Cardiopulmonary bypass was achieved by means of a rotating disc oxygenator. It is clear that any method of coronary perfusion suitable for open surgical treatment of aortic stenosis would be equally applicable in the direct attack on regurgitation. Actually, coronary ostial cannulation is more easily accomplished in the dilated aortic ring than in patients with aortic stenosis. All combinations of stenosis and insufficiency may be encountered; in fact, the need for time to correct postvalvulotomy regurgitation was a prime factor in the trend away from hypothermia.

RETROGRADE CORONARY PERFUSION

Accepting the premise that some kind of coronary perfusion was essential, we turned first to retrograde perfusion of the coronary sinus. Lillehei and his associates[16] are properly credited with the first clinical trial of retroperfusion to achieve direct view of the aortic valve. Initially, the patulous coronary sinus was cannulated with a plastic catheter which was then sutured into position to prevent dislocation during the operative procedure on the aortic valve. The most attractive feature of retrograde perfusion is that the coronary circulation, though reversed, is never interrupted since the necessary cannulation is effected via atriotomy during cardiac perfusion from the heart-lung apparatus. Blood flows from a reservoir into the coronary sinus as soon as the aorta is occluded and incised distal to the valve. Distance from the reservoir to the heart is usually held at 50 to 75 cm. The reservoir is transfused from the arterial limb of the heart-lung machine so that warm, oxygenated blood is always available. Some recent work by Berne, Jones, and Cross[17] suggests that cold blood may be acceptable, but our experience with this is accidental, when blood approached room temperature due to early filling of the reservoir, and no conclusions can be drawn.

Proximity of the atrioventricular node to the coronary sinus warns against suture fixation of whatever cannula is used for the perfusion. Clinically, gross and persistent conduction aberrations have resulted from such a maneuver. The logical alternative to suture-fixation is use of a No. 10 to No. 18 Fr. Foley catheter with a 5 c.c. balloon. Inflation of the balloon with blood or saline solution prevents escape of the catheter from its wedge position in the coronary sinus. The anterior coronary and Thebesian veins are available to transport blood into the cardiac chambers after the Foley balloon is distended but before the onset of retrograde coronary perfusion. This technique was used in numerous dog experiments with consistent and interesting results. The flow rate for each retroperfusion was between 35 and 55 c.c. per minute. The method is depicted in Fig. 1.

Although animal survival was the rule, certain disadvantages appeared inseparable from the method. A considerable amount of arterialized blood escaped into the right atrium and right ventricle, failing to complete the route through the capillary bed. This fraction of the perfusate was totally denied to the myocardium. Another clear disadvantage was the very small volume of blood emanating from the right coronary ostium. This indicated the left side of the heart was perfused to the near exclusion of the right. Gregg[18] would have predicted this phenomenon from his exhaustive studies of the coronary circulation. The third and most striking disadvantage lay in the behavior of the heartbeat during retrograde coronary perfusion. The heart would approach standstill; then, as though the heart were shifting gears, the rhythm returned to the modulated vigor characteristic of the heart during cardiopulmonary bypass. Color of the myocardium remained pink in most experiments. In one animal, complete heart block preceded the routine episode of severe bradycardia. This borderline standstill developed in each animal just after reversal of the coronary circulation.

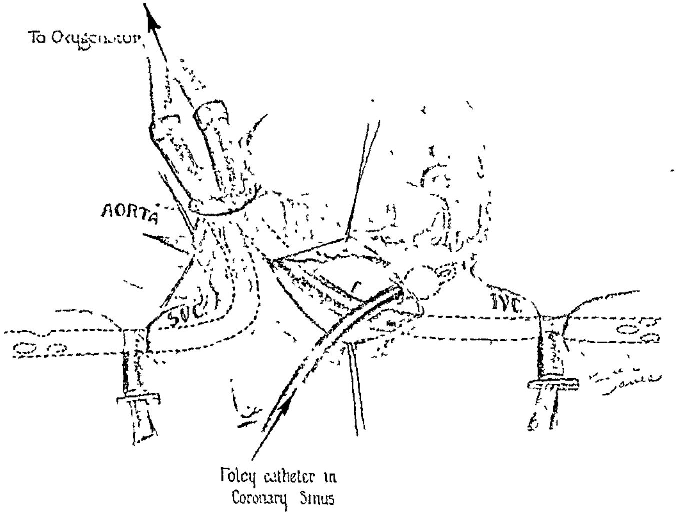

Fig. 1.—An acceptable method for retrograde coronary perfusion.

Postmortem studies in 2 animals were sufficient to strengthen the impression that something other than retrograde coronary perfusion was the answer to the general problem. A huge ulcer and associated thrombus congruent with the site of the Foley balloon obstructed completely the coronary sinus—right atrial junction in one dog. In the other, similar but less striking changes were observed. The possibility that acute and total occlusion of the coronary sinus may not be serious detracted little from our disappointment in noting that balloon fixation was not unattended by complications.

Duration of retroperfusion was 15 minutes. The perfusate was aspirated and discarded. Flow rates for the body perfusion varied from 65 to 85 c.c. per kilogram per minute.

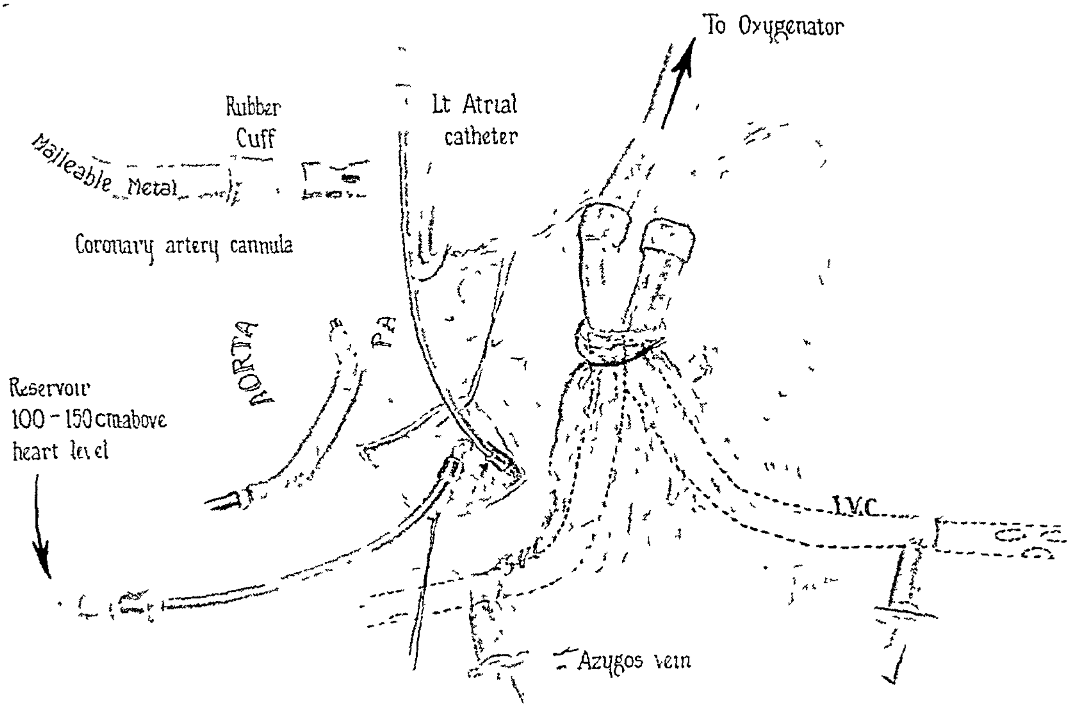

Fig 2—Individual cannulation of the coronary ostia Inset shows detail of cannula

CORONARY OSTIAL PERFUSION

In turning from retrograde to forward coronary perfusion, the first problem was selection of an appropriate catheter. Studies of the anatomy of the coronary ostia in dogs revealed that in most animals the right coronary ostium was very small, essentially precluding direct cannulation. The left coronary artery frequently trifurcates immediately below the aortic surface thereby preventing any considerable length of cannulation. The catheter, therefore, could not be wedged into the coronary artery, and the need for constant control of the catheter tip indicated that some relatively inflexible material would best meet this requirement. The matter of catheter type suddenly became an important consideration. The design of the malleable metal catheter ultimately evolved is seen in Fig. 2. The rubber cuff prevents reflux of arterialized blood into the operative area, and extra holes in the catheter tip tend to avert obstruction due to changing angulation of the instrument. Another advantage to malleable metal is the fact that cannulation is accomplished almost instantaneously with visualization of the ostia. No additional forceps is needed to manipulate the cannula into the coronary vessel. The catheter is coated with silicone as are all metal, glass, and rubber surfaces in the extracorporeal heart-lung circuit.

Gravity flow over a distance of 100 to 200 cm. suffices to propel blood from a reservoir into the artery. The flow rate varied from 25 to 50 c.c. per minute, and duration of coronary perfusion was 15 minutes. Only the left coronary artery was perfused. The quality of heartbeat was much improved over that observed with retrograde perfusion, certainly an expected finding. Ventricular fibrillation did not occur in any experiment. At the outset we were concerned lest fibrillation be stimulated by whatever potential develops at the interface of oxygenated and nonoxygenated myocardium. The work by Brofman, Leighninger, and Beck[19] would indicate that ventricular fibrillation might be expected, particularly upon resumption of total cardiac perfusion. No serious arrhythmias were noted.

Anatomic studies in man showed that forward perfusion with individual cannulation of both coronary ostia could be easily performed. Fig. 2 shows cannulation of both vessels, which would be advisable in human beings though nearly impossible, and perhaps unnecessary, in the dog. The ascending aorta in man fortunately is easier to work with than in dogs. One animal was lost from delayed hemorrhage at the aortic incision after a procedure remarkable for its difficulty in closing the aortotomy.

A point we believe to be of paramount importance is the use of a left atrial catheter to empty the left side of the heart. Visualization and cannulation of the coronary ostia is accomplished with great dispatch if a left atrial catheter is employed. Furthermore, at the conclusion of the procedure the left heart may be filled with blood or saline solution by means of the catheter to ensure displacement of all air. In dogs, we introduced a No. 18 Fr. plastic catheter into the left atrium through a pulmonary vein, the blood was returned to the oxygenator via the coronary drainage attachment. Decompression of the left side of the heart is essential when no septal defect exists. The operative field is nearly bloodless with removal of left atrial input.

SUMMARY AND CONCLUSIONS

While the several forms of elective cardiac arrest may be applied to the surgical treatment of congenital aortic valvular disease under direct vision, some kind of coronary perfusion is necessary for the exposure of acquired diseases. Hearts with greatly decreased reserve are intolerant of any known type of arrest. Retrograde perfusion of the coronary sinus provides continuous myocardial oxygenation. Unfortunately, coronary sinus perfusion reaches principally only the left side of the heart, and the problem of cannula fixation remains incompletely solved. Distortions in the heartbeat induced by reversal of the coronary circulation also detract from the use of this technique.

Individual cannulation of the coronary ostia, after prompt emptying of the heart by means of the left atrial catheter, supplies an acceptable method for maintenance of cardiac circulation during direct approaches to the aortic valve. If anything, aortic insufficiency provides an easier field in which to work than does stenosis. A malleable metal, siliconized cannula with rubber cuff and multiple holes in the tip is suggested as an appropriate instrument for direct coronary ostial perfusion.

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SCOLIOSIS AND HERNIATION AFTER OSTEOPLASTIC THORACOPLASTY

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Since the introduction of osteoplastic thoracoplasty in 1952, it has been performed by us in 200 cases. The technique has been taken up in many chest centers especially in Europe. Compared with other space diminishing methods of the thoracic cavity as an addition to pulmonary resection for tuberculosis, it has the following advantages: (1) The size of the thoracic cavity can be tailored to fit the remaining lung parenchyma. (2) The fixation of ribs will leave a stable chest wall without paradoxical movements; thus, coughing is effective and ventilation unimpaired. The osteoplastic thoracoplasty can therefore be performed at the end of the pulmonary *resection without increasing the risk for the patient. The advantage of a* one stage procedure is obvious. (3) The decrease in size of the thoracic cavity obtained at operation is permanent. (4) The functional result, both as regards pulmonary function and arm movements, is excellent. The cosmetic result is excellent and the deformity encountered is practically only visible in the axilla when the patient elevates his arms.

The aim of this paper is to emphasize important technical details and to report scoliosis and herniation of the lung in 104 patients from one to 5 years after the operation.

HERNIATION OF THE LUNG ABOVE THE ROOF

The aim of the osteoplastic thoracoplasty is to obtain a permanent decrease of the thoracic cavity. Therefore, certain steps are taken to prevent a herniation of the lung above the roof.

1. The second rib is made as short as possible; thus, it will be straighter and it can be placed as close as possible to the mediastinum.

2. The costal cartilage is incised, facilitating fixation of the second rib to the mediastinum. This is a very important technical detail not performed in the beginning. When herniation was detected in some of the earlier cases

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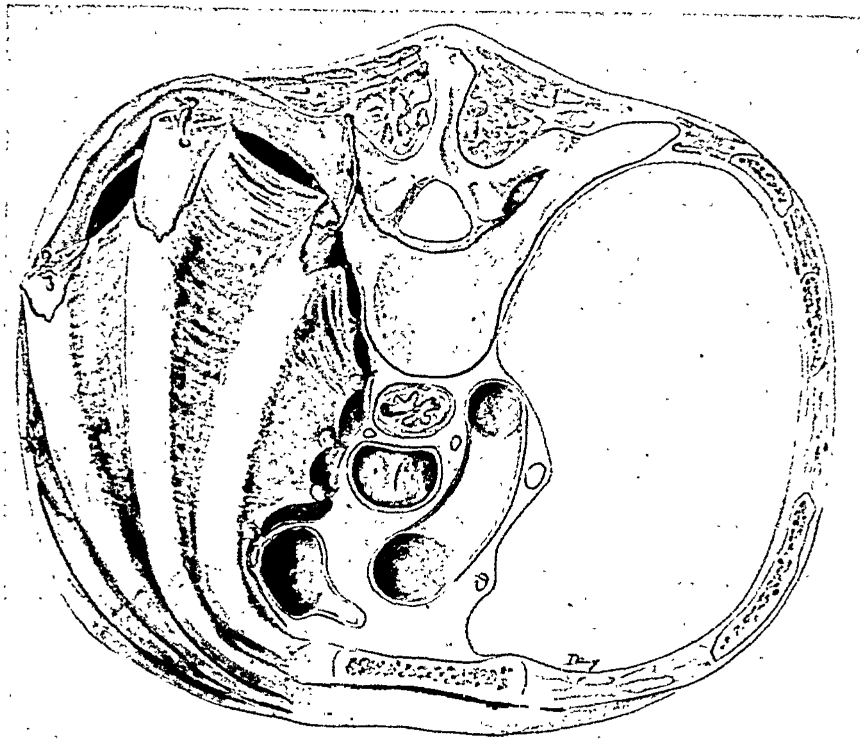


Fig. 1.—In the beginning, the second rib was bent in the costal cartilage and therefore a larger space resulted anteriorly between the rib and mediastinum causing herniation in many cases.

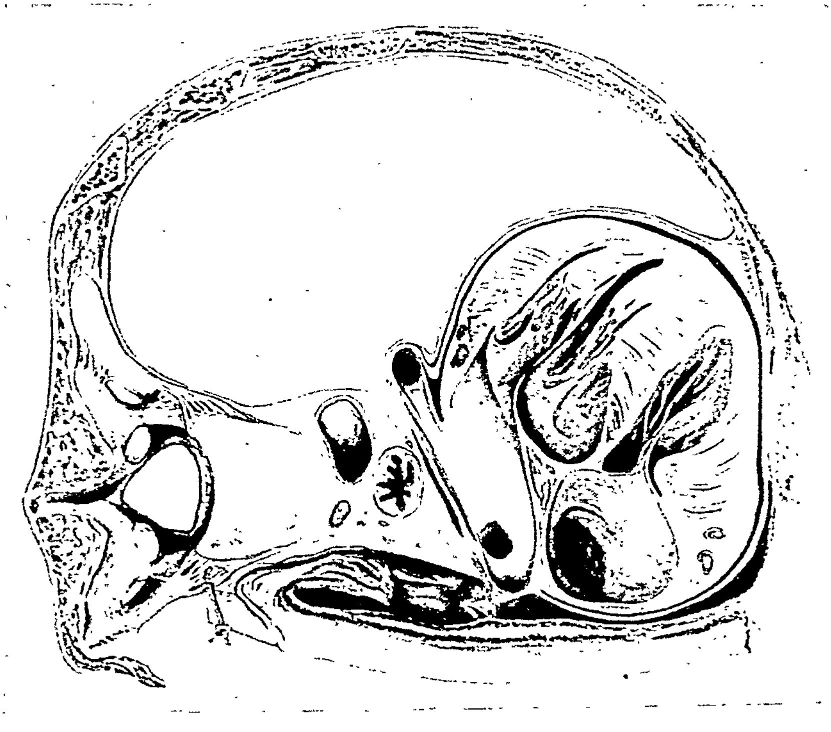


Fig. 2.—When the cartilage was incised anteriorly it was possible to place the second rib close to the mediastinum, preventing herniation.

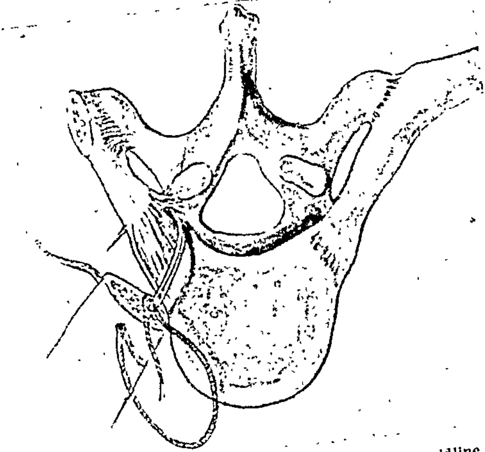
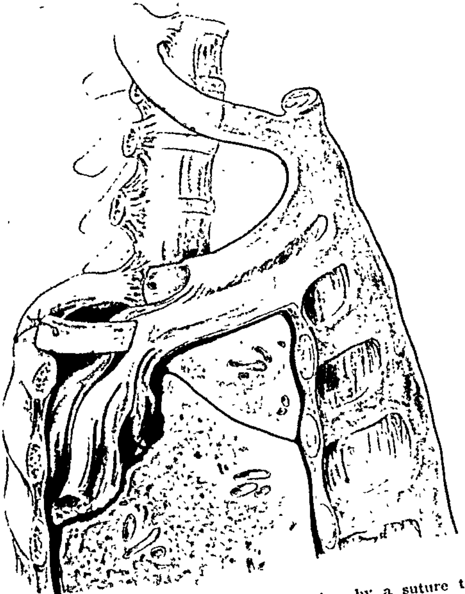


Fig. 3.—The posterior end of the rib is fixed as close to the midline as possible, i.e., by a suture through the costovertebral ligament.



by a suture through

and found to be anteriorly, this step was added and was found to decrease the incidence of herniation (Figs. 1 and 2).

3. The posterior end of the second rib is fixed by a nylon thread through a drill hole and then to the costovertebral ligament (Figs. 3 and 4).

4. The intercostal muscle bundle left on the top of the second rib is fixed to mediastinal tissue by a row of intercostal sutures, thus closing the roof of the chest medially (see Fig. 1).

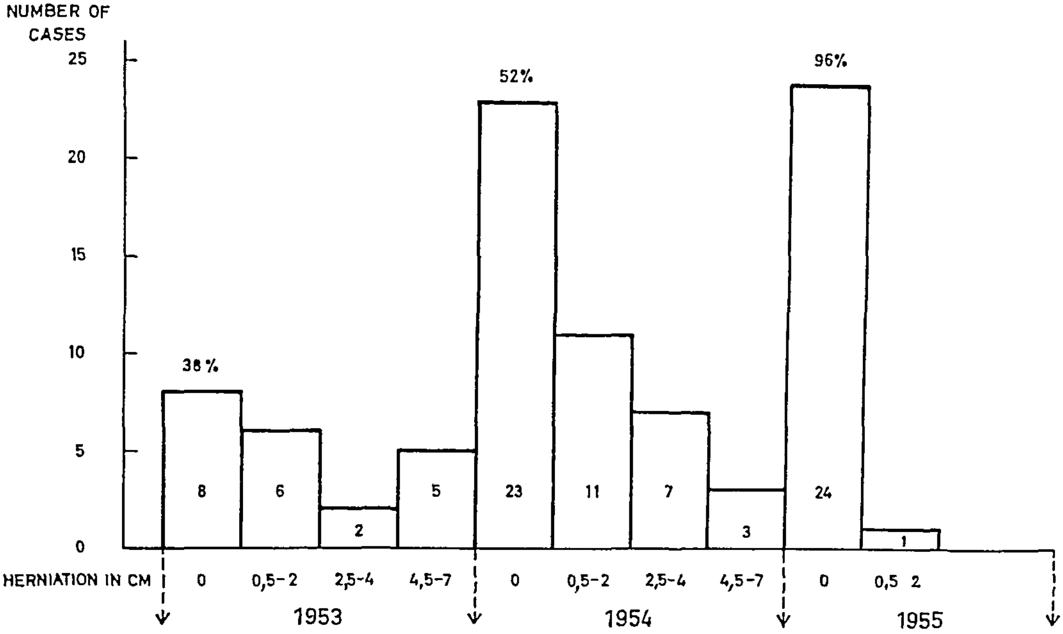


Fig. 5—Diagram of the degree of herniation found in cases from the different years demonstrating the importance of technical details in preventing herniation

Of the 104 cases investigated, 17 had the first rib removed, in all the other cases the first rib was left in place. There was the same incidence of herniation whether the first rib was left in place or not. Furthermore, the same incidence of herniation was found if the operation was carried out on the left or right side

In the whole material the following degree of herniation was found:

No herniation	64%
The lung 0.5 to 2 cm. above the roof	19%
The lung 2.5 to 4 cm. above the roof	9%
The lung 4.5 to 7 cm. above the roof	8%

Fig. 6—A roentgenogram of a 57-year-old man, who has had a right upper lobectomy and osteoplastic thoracoplasty. The second rib was not placed as close to mediastinum as possible, resulting in a big herniation The hernia was 7 cm above the roof There was a tracheal deviation of 2 cm and a scoliosis of 1 cm. over to the right side The diaphragmatic movement was 5 cm on the right and 7 cm on the left side

Fig 7—A roentgenogram of a 42-year-old woman, who had had resection of the superior lobe and superior segment of the lower lobe on the right side with an osteoplastic thoracoplasty After 3 years this x-ray film was taken which demonstrates no herniation A scoliosis of 2 cm, and deviation of the trachea of 4 cm over to the right side The right side of the diaphragm moved 6 cm, while the left side moved 7 cm Bronchospirometry showed an oxygen uptake of 23 per cent on the right side

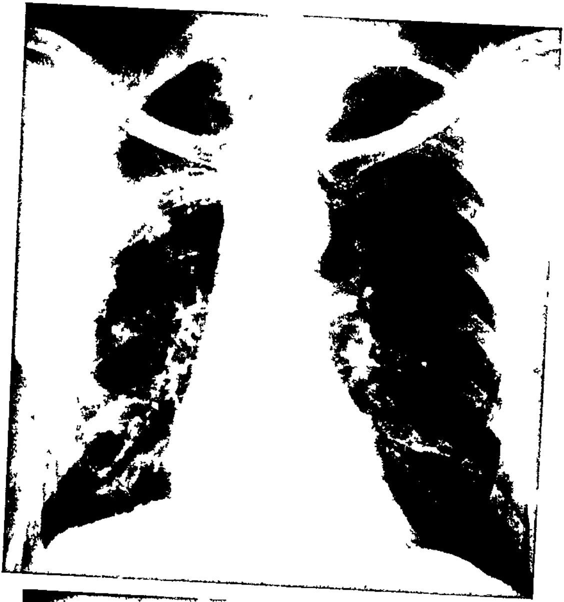


Fig 6

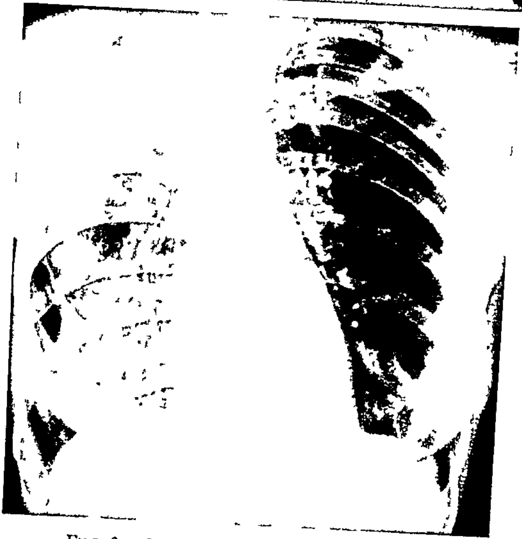


Fig 7

Figs 6 and 7—*For legends see opposite page*

Fig. 8.

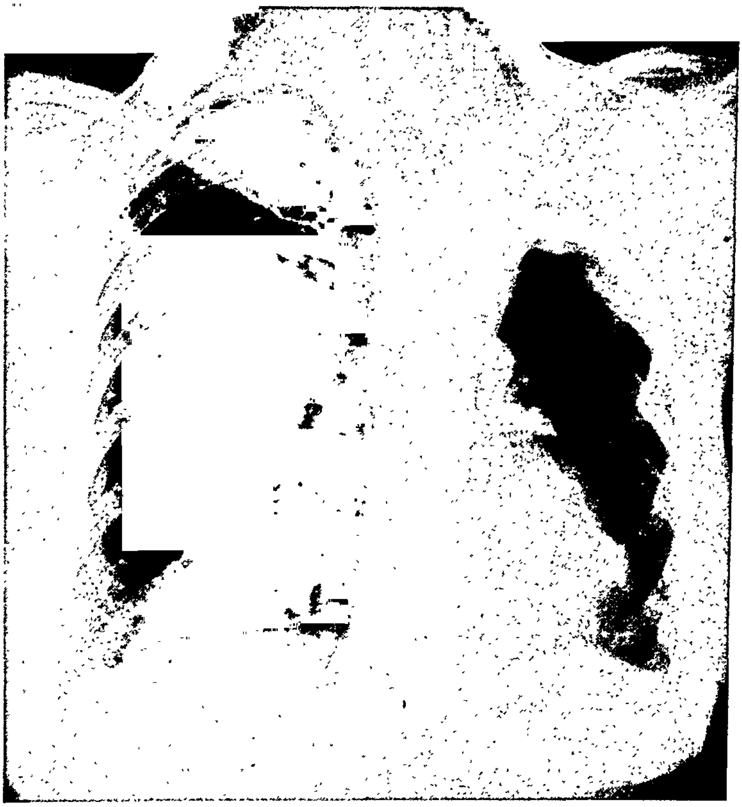
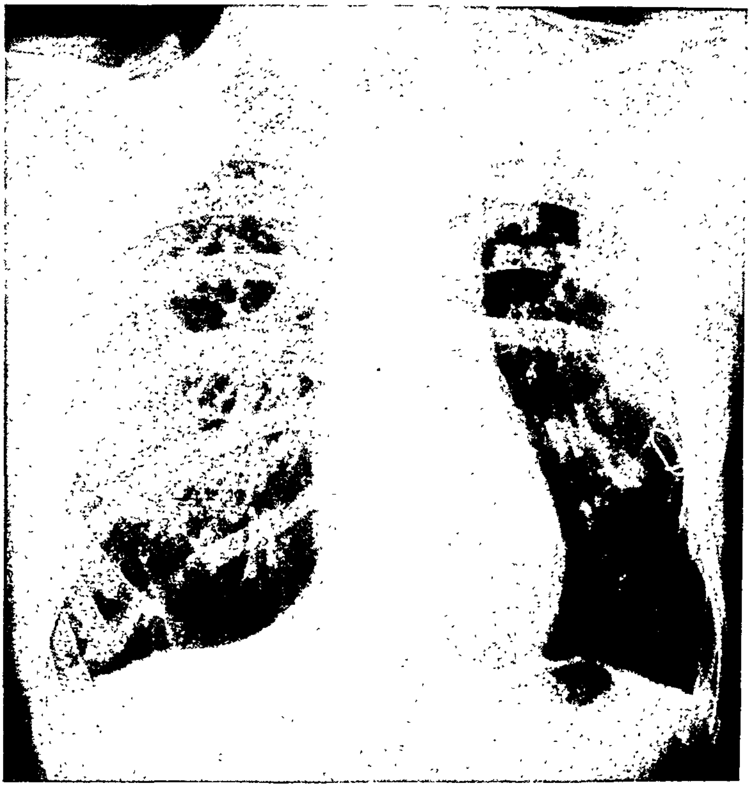


Fig. 9.



Figs. 8 and 9.—*For legends see opposite page.*

As some of the above mentioned technical details were worked out during 1953, and the final technique adopted during 1954, it is interesting to see how important these technical details are in preventing herniation Of patients operated on in 1953, only 38 per cent were without herniation, in the ones from 1954, 52 per cent, while in the cases from 1955 as many as 96 per cent were without herniation The degree of herniation in cases from the different years will be shown in Figs 5 10

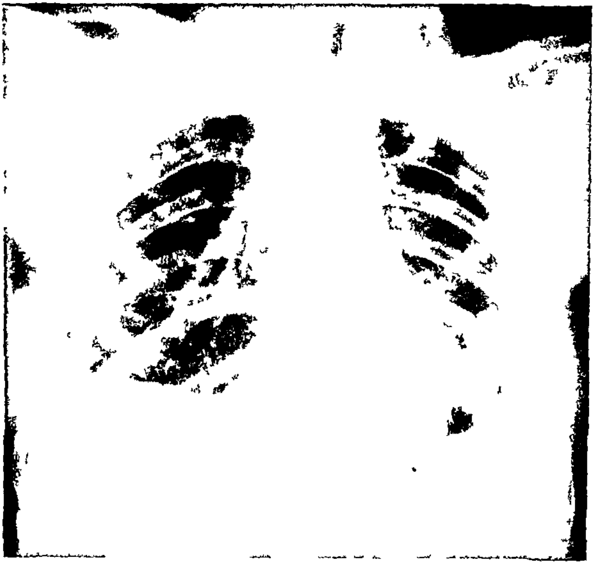


Fig 10—This x ray film is of a 42 year old man who has had bilateral resections with osteoplastic roof thoracoplasties on both sides There is no herniation on either side The first rib is left intact on both sides There is a scoliosis of 1 cm to the right side a tracheal deviation of 1 cm to the right side The diaphragm moves 7 cm on the right and 6 cm on the left side Three years after the operation the patient is in an excellent condition working full time Oxygen uptake on the right side 57 per cent on the left side 43 per cent. Ventilation on the right side is 56 on the left 44 Sputum and gastric washings are negative by guinea pig test

It can, therefore be concluded that if the technique is followed in detail there will be a negligible incidence of herniation of lung above the roof

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Fig 8—An x ray film of a 39 year old woman who had had resection of the superior lobe and the superior segment of the lower lobe on the left side plus osteoplastic thoracoplasty After 3 years of observation there was no herniation above the roof a scoliosis of 2 cm and a tracheal deviation of 2 cm over to the left side The left side of the diaphragm moved 6 cm while the right side moved 8 cm

I of a 41 year old man who had had a right conventional
thorac years previously The film shows a re expansion of the right
upper On the left side on the other hand the film shows the results
of a terior and anterior segments of the left upper lobe plus the
superior segment of the lower lobe with an osteoplastic thoracoplasty performed 4 years previously Four years after this operation there is no herniation above the roof there is no scoliosis but a tracheal deviation of 1 cm over to the left The left and right sides of the diaphragm move equally 5 cm

SCOLIOSIS

There was no difference in the degree of scoliosis whether the first rib was left in place or resected. To measure the amount of scoliosis, a line was drawn on the frontal roentgenogram between the midpoint of the first and twelfth thoracic vertebra.

The maximal deviation from this line was measured and the following values obtained:

No scoliosis	13%
0.5 to 1 cm. deviation	43%
1.5 to 2 cm. deviation	36%
2.5 to 3 cm. deviation	8%

Some scoliosis was therefore found in 87 per cent of the cases. In most of these cases there was only a slight scoliosis, 43 per cent. A moderate scoliosis was encountered in 36 per cent. A severe scoliosis was only found in 8 per cent.

Tracheal Deviation.—The tracheal deviation was measured in centimeters from the same line between the first and the twelfth thoracic vertebra used for calculation of the scoliosis. Usually there was a tracheal deviation to the operated side.

The tracheal deviation was found to be somewhat smaller if the first rib was resected on the right side, on an average of 1.8 cm. as compared with 2 cm. for cases where the first rib was left behind. The corresponding values on the left side were 1.1 cm. when the first rib was resected and 1.7 cm. when it was left behind.

Furthermore, there was less tracheal deviation if the patient was operated upon on the left side. This is to be expected as the position of the aorta will diminish the deviation of the trachea to the left side. The deviation of the trachea was always to the side of operation with the exception of one case in which a contralateral fibrothorax kept the trachea fixed 2 cm. to the opposite side of the operation.

There was some correlation between the tracheal deviation and the scoliosis. A more pronounced scoliosis was usually accompanied by a greater deviation of the trachea (Table I).

TABLE I. THE CORRELATION BETWEEN THE SCOLIOSIS AND THE DEVIATION OF TRACHEA AFTER AN OSTEOPLASTIC THORACOPLASTY

NO. OF CASES	SCOLIOSIS (CM.)	TRACHEAL DEVIATION (CM.)	
		AVERAGE	RANGE
13	0	1.3	0-2.5
39	0.5-1.0	1.4	0-3
39	1.5-2.0	2.0	0-4
8	2.5-3.0	2.3	1-3

Diaphragmatic Movements.—No severe impairment of the diaphragmatic movements was encountered after pulmonary resection with an osteoplastic thoracoplasty. After right-sided operation, the maximal diaphragmatic movements were on the right side on an average 4.5 cm., range from 2 to 9.5 cm., as compared with an average of 5.6 cm., range from 2 to 9 cm. After a left-sided operation, the left diaphragm moved on an average of 4.6 cm., range from 2 to 7 cm., as compared with the right which on an average moved 5.8 cm., range from 3 to 10 cm.

SUMMARY

A follow-up study has been carried out on 104 patients undergoing pulmonary resection with an osteoplastic thoracoplasty in order to estimate the degree of scoliosis, herniation, tracheal deviation, and the diaphragmatic movements. In the beginning, a herniation of the lung above the roof was encountered rather frequently. When the technique was further developed, with incision in the second costal cartilage and a fixation of the second intercostal muscle bundle to the mediastinal pleura, the incidence of herniation became negligible.

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FUNCTIONAL STENOSIS DUE TO BRONCHIAL ANGULATION

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A SIGNIFICANT consideration in determining the extent of pulmonary resection for tuberculosis is the presence or absence of bronchial stenosis. Functional stenosis due to kinking of the bronchus by extrinsic disease may resemble endoscopically the fixed stenosis due to intrinsic thickening.

Björk in a series of 1,000 resections reported 4 cases with a diagnosis of apparent bronchial stenosis. They were associated with lower lung field disease causing a "dislocation of the lung by pleural effusion and fibrosis." At exploration, one with bronchotomy, the apparent stenosis was found to be due to simple kinking of the bronchus.

In a series of 200 resection cases, we noted 4 patients with destroyed left upper lobes who showed bronchial angulation which simulated anatomic stenosis at the time of preoperative bronchoscopy. On first inspection of the bronchus, it appeared that intrinsic stenosis was present and that pneumonectomy would be indicated. Such a course was to be avoided if possible as these patients generally have contralateral disease and a limited pulmonary reserve. To preserve the large volume of parenchyma in the lower lobe, it was important to recognize that the deformity was due mainly to extrinsic factors.

Bronchograms of 3 of these, and of another who refused surgery, illustrated the typical deformity pictorially (Fig. 1). The characteristic finding was a left main bronchus which curved outward and then upward, leading directly into the upper lobe orifice rather than the lower. The lower lobe took off from this upward curve in a sharply posterior and downward direction, producing marked angulation. Tuberculous bronchiectasis was present in the upper lobe in each case, and in the superior segment in one. No significant basilar bronchiectasis due to poor drainage was evident. Serial tomograms showed that the bronchial deformity was not present during the acute stage of the disease but developed as the destroyed left upper lobe contracted.

The sputum was persistently positive and resistant to isonicotinic acid hydrazide and streptomycin in 3 cases at the time of surgery. The pulmonary findings by x-ray and exploration in each case were those of a contracted,

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destroyed left upper lobe with open cavitation, an overdistended lower lobe, and pleural and peribronchial fixation by fibrosis. A left upper lobectomy, with combined superior segmentectomy in one, and an attempt to free the angulated bronchus was carried out in each case. The postoperative course was complicated in 2 cases by bronchopleural fistula, in one by staphylococcal empyema, and in one by atelectasis. Postresection thoracoplasty was added in each. These patients recovered slowly but completely.

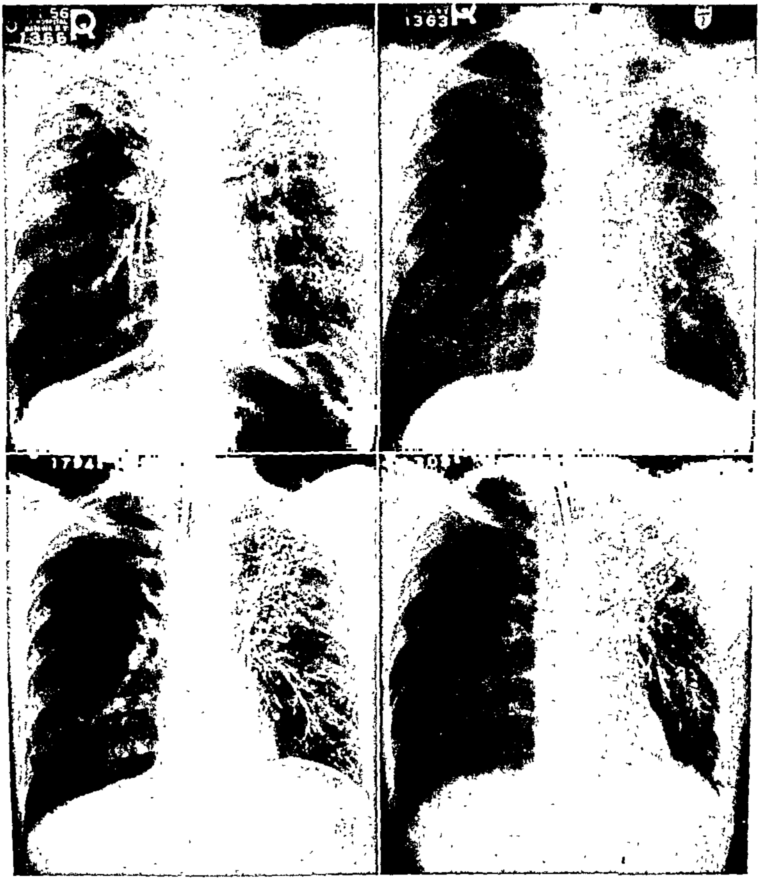

Fig. 1.—Bronchograms of 4 patients which illustrate upper lobe cavitation and bronchiectasis associated with angulation of the lower lobe take-off.

During a 2- to 4-year follow-up, x-ray studies have revealed a stable lung and no positive cultures have been obtained. Results are considered good for control of the tuberculosis. Recent bronchograms of 3 patients show partial correction of the functional stenosis and no evidence of basilar bronchiectasis. One patient has developed cylindrical stenosis of the lower lobe bronchus. Clinically, they have all been quite free of cough or sputum production.

SUMMARY

A destroyed, contracted left upper lobe may be associated with sufficient angulation of the lower lobe bronchus to cause functional stenosis. This is easily confused endoscopically with the anatomic stenosis produced by intrinsic bronchial disease. Recognition of this condition may allow conservation of pulmonary tissue at operation. Four such cases are reported.

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RUPTURES IN THE BRONCHIAL TREE DUE TO BLUNT TRAUMA

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Much progress in the handling of chest injuries has occurred since the beginning of World War II. Similarly many improved surgical and anesthetic techniques have been developed to help cope with the more serious injuries, such as those to the trachea and bronchi.

Blunt injuries to the thorax have been implicated as the cause of many pathologic states: diaphragmatic lacerations, intrapulmonary hematomas, and cavities, lacerations of the great vessels and ruptures of the trachea or bronchi. The latter type of injury has been rather rare. Nevertheless, it is becoming apparent that with early diagnosis and proper management, patients with these injuries can be restored to full activity.

A review by Kinsella and Johnsrud in 1947[1] demonstrated a 33 per cent mortality associated with these conditions. Secondary repair in patients who luckily survive the injury is extremely difficult and plagued by the problems of bronchostenosis and grafting. It is obvious that ideal treatment would be prompt surgical repair. We have found only three reports of successful primary operations. Griffith[2] reported such an operation in 1949, Scannell[3] primarily repaired a laceration of the thoracic trachea, reporting it in 1951. Richards and Cohn[4] reported a similar case in August, 1955. These patients are indeed desperately ill but when anesthesia is skillfully handled corrective surgery can be accomplished. Recent experiences with 2 desperately injured patients justify this point of view.

CASE REPORTS

CASE 1.—A 25 year old airman was struck by the steering post of his automobile in a head on collision. He received emergency treatment at a nearby hospital, where he was found to have severe dyspnea with extensive subcutaneous emphysema over neck, chest, abdomen, and arms. A right tension pneumothorax was present; a small catheter was inserted into the right chest and connected to the underwater seal bottle (Fig. 1). As leakage of air was tremendous and continuous even during expiration, a bronchial tear was suspected. The patient was quickly transported to a general hospital, where bronchoscopy was performed under topical anesthesia. The bronchoscope passed into the mediastinum through a rent at the bifurcation of the trachea. As visualization was

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impaired, the scope was quickly withdrawn. The patient was adequately ventilated with oxygen and was then rapidly intubated, utilizing minimal amount of Pentothal followed by Anectine. A Carlen's endobronchial catheter was utilized, enabling the anesthesiologist to ventilate either lung and proved to be of great value in the almost constant bronchial aspiration that was necessary to remove the secretions. A standard right thoracotomy

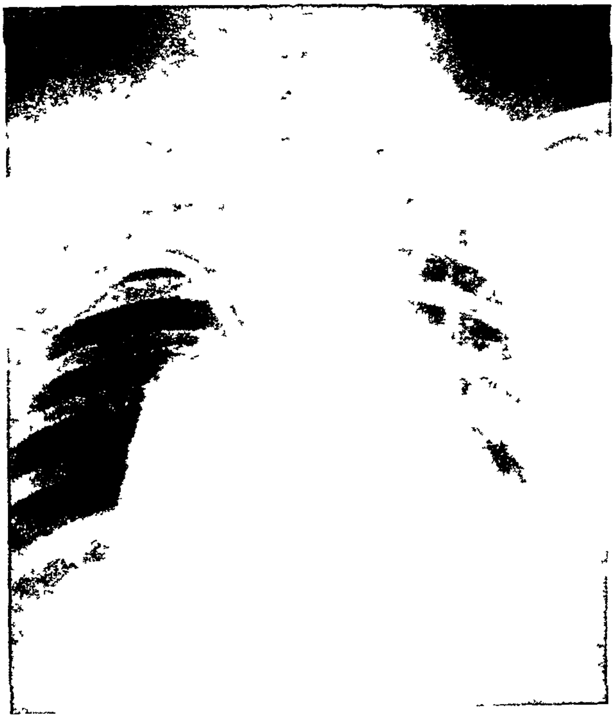

Fig. 1—Case 1. Preoperative x-ray film

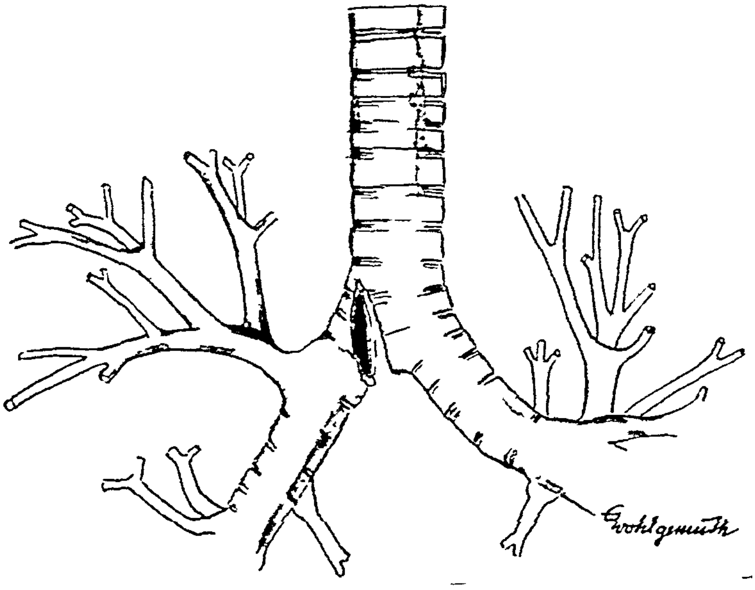

Fig 2—Case 1. Tracheal tear

was performed. On entering the chest, a tension pneumothorax (present despite the catheter drainage) was relieved. Air escaped violently into the pleural cavity from an opening into the mediastinum between the inferior and superior pulmonary veins. This was tamponaded with a lap pad to permit partial inflation of the right lung. The posterior mediastinum was opened and the azygos vein divided, exposing the trachea. The circumferential tear through the carina had almost completely separated the right main stem from the trachea (Fig. 2). The Carlen's catheter was inserted into the left main bronchus, its balloon inflated, and the trachea repaired with interrupted fine silk sutures.

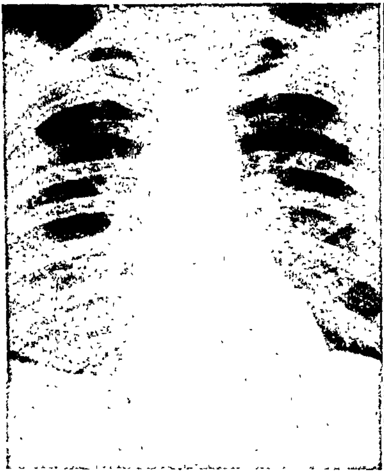
Fig. 3.

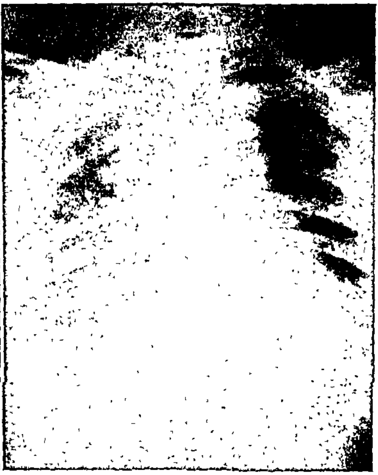
Fig. 4.

Fig. 3.—Case 1. Postoperative x-ray film.
Fig. 4.—Case 1. Late postoperative x-ray film.

It was noted that the right lung felt extremely crepitant. This was a coarse crepitus, similar to that felt in the skin. A fair degree of interstitial emphysema was presumed to be present. The anesthesiologist commented upon the resistance of the lungs to his manual ventilation despite a clear airway. The chest was closed with underwater-seal catheter drainage and a tracheotomy was performed (Fig. 3). The patient gradually became less and less short of breath during the week following operation. He was bronchoscoped one month following surgery (Fig. 4). The trachea was then well healed with no evidence of stenosis. The patient was returned to full duty.

Case 2.—This patient sustained a similar blunt injury in an automobile accident. He was hospitalized promptly and found to be severely dyspneic with emphysema of the neck, shoulders, left side of the chest and abdomen. A tracheotomy was performed. However, dyspnea did not abate and emphysema became more widespread. A left pneumothorax was noted. A catheter was placed anteriorly in the left chest and a tension pneumothorax partly relieved. The right lung remained fully expanded throughout the course. Consultation was then obtained as the patient did not improve. Twenty-four hours after injury the patient was operated upon. After a small dosage of Pentothal and Anectine, a Carlen's catheter was rapidly inserted into the trachea and the left chest opened through a standard incision. A tension pneumothorax was present. The patient had sustained a deep laceration of the lingula, tearing a segmental branch from which a sizable air leak occurred. A small intrapulmonary hematoma was present in the lower lung. In addition, the lung was extremely crepitant, again indicating interstitial emphysema. The anesthesiologist again commented on the difficulty of ventilating this patient. The torn bronchus was ligated and covered with adjacent pulmonary parenchyma. Throughout this manipulation, the anesthesiologist experienced difficulty in clearing the left-main stem bronchus of dark blood. As exploration of the mediastinum (carina and main-stem bronchus) showed no further damage, the chest was closed after insertion of catheters. The tracheotomy wound was opened and a small thyroid ima artery was found to be open and bleeding into the trachea. This was ligated and a tracheotomy tube was re-inserted as the Carlen's catheter was withdrawn. As expected, the patient was improved, but still dyspneic for several days following surgery. However, he eventually made a very satisfactory recovery from his injury.

SUMMARY

It is our firm belief that prompt clinical recognition of bronchial tears permitted successful surgery in these patients. The presence of subcutaneous emphysema, dyspnea, and tension pneumothorax were the presenting symptoms and the key to diagnosis. Early operative efforts were rewarded by good healing without serious sequelae (stenosis, atelectasis, and infection). The Carlen's catheter was most useful in permitting ventilation of one lung while the other was out of the surgical field. The successful anesthetic management in each case, rapid intubation under Pentothal and Anectine anesthesia lent itself well to the problems at hand. The presence of interstitial emphysema in the lungs was noted with interest. Certainly it delayed return of adequate ventilation for several days following surgery and tracheotomy was most helpful in this critical situation.

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A NEW TECHNIQUE FOR THORACOTOMY AND CHEST CLOSURE IN THE EXPERIMENTAL ANIMAL

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chondral union, and 2 "floating" anteriorly. Despite the fact that the dog has a greater number of ribs attaching to the sternum, his costochondral attachments and therefore his entire rib cage are more flexible than man's. This greater flexibility is an anatomic adaptation to the dog's need for a proportionately greater vital capacity to accommodate running. It is this same greater costochondral flexibility that allows wide intercostal exposure in the thoracotomy without the need for rib resection.

2. *Clavicle:* In the dog there is no clavicle interposed between the acromion of the scapula and the manubrium sterni. In forming the anterior portion of the shoulder girdle in man, the clavicle has nearly a dozen muscular and ligamentous attachments. With the absence of the clavicle in the dog, the anatomic relationships of these attachments are distinctly altered.

Muscular.—

1. *Scalenus:* In both dog and man, the scalenus is primarily an accessory *muscle of inspiration, arising from the transverse processes of the lower 4* to 6 cervical vertebrae. As in the human being, the scalenus of the dog forms three distinct muscle bundles, *anticus, medius,* and *posticus.* In man, the scalenus *anticus* and *medius* insert on the inner and upper surfaces of the first rib, respectively, while the *posticus* inserts on the outer surface of the second rib. In the canine, the *anticus* (*scalenus primae costae*) similarly inserts onto the first rib. The *posticus* of the dog, however, has its inferior attachment on the fourth rib. Most important for this discussion is the *medius,* the largest and longest portion of the scalenus, which inserts onto ribs 5 through 9 via an extensive aponeurosis partly hidden by the overlying *external abdominal oblique.*

2. *Serratus anterior (ventralis):* In man, this muscle is a thin muscular sheet arising by fleshy digitations from the outer surface and superior borders of the upper 8 or 9 ribs, and inserting onto the vertebral aspect of the scapula. Its action in man is primarily rotation of the scapula as occurs with raising and lowering of the shoulder and with pushing. In the dog, the serratus anterior is much more highly developed and more powerful, since the right and left serratus muscles form a muscular "sling," supporting the weight of the trunk onto the pectoral limbs, especially during running or leaping. For this greater function the muscle has a greater trunk distribution, arising from the transverse processes of the lower 5 cervical vertebrae as well as from the lateral surfaces of the upper 8 or 9 ribs.

3. *Rectus abdominus:* In both man and dog, this muscle originates at the pubic crests. In man, the rectus extends superiorly to insert on the anterior cartilaginous portions of ribs 5, 6, and 7. In the dog, the rectus traverses the entire thoracic cage to insert superiorly onto the first rib. This longer distribution in the dog allows the rectus to aid in the advancement of the hind limbs during gallop.

Some of the more important relationships of these muscles are depicted in Fig. 1. Occasionally variations from the normal will occur. In two experiments, for example, the scalenus medius had its insertion begin on rib 6 rather than rib 5. Since this muscle is a particularly important landmark, its exact distribution should be ascertained in each instance. It should be noted, furthermore, that the *latissimus dorsi,* the *external abdominal oblique,* and the *intercostal muscles* of the dog are essentially similar in origin, distribution, and function to the corresponding muscles in man.

THE THORACOTOMY

Anesthesia is induced by intravenous sodium Pentothal, and an endotracheal tube is inserted and connected to a suitable respirator. The dog is placed in the completely lateral position, with a pack of towels, 2 or 3 inches in thickness, inserted under the table side of the animal. This arches the operative side into better view, and allows the shoulder girdle to fall forward out of the field of incision.

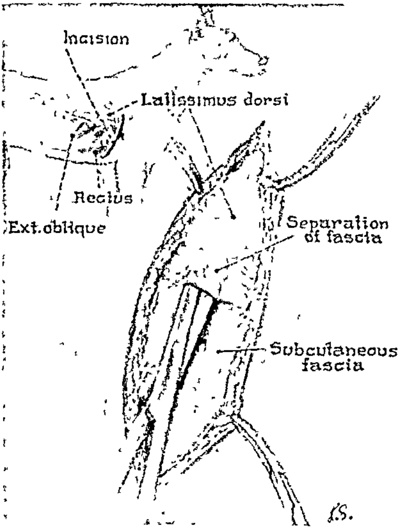

Fig 1—The skin and subcutaneous tissue are incised A small incision is made in the subcutaneous fascia at its function with the latissimus dorsi

The ribs, the latissimus dorsi, and rectus abdominus are palpated and the area of the fourth intercostal space is identified. Incision is made through the skin and subcutaneous tissue over the fourth intercostal space, some 12 cm. in length, and extending from approximately 4 cm. dorsal to the lateral border of the latissimus dorsi ventrally to the lateral border of the rectus abdominus. At this juncture the lateral border of the latissimus dorsi is identified occupying the upper one third to one half of the wound bed (Fig. 1) with the subcutaneous fascia extending ventrally from its lateral margin.

A small incision, 1 cm. in length, is made in the subcutaneous fascia at its junction with the latissimus dorsi. Both index fingers are inserted into this opening and by gentle traction in opposite directions (cephalad and caudad) the fascia is separated from its muscular attachment.

Three important landmarks are now seen (Fig. 2, *A*): (1) the long and narrow scalenus medius, (2) the large digitations of the serratus anterior above the scalenus, and (3) the thin superior margin of the external abdominal oblique overlying the beginning of the scalenus medius insertion onto the fifth rib.

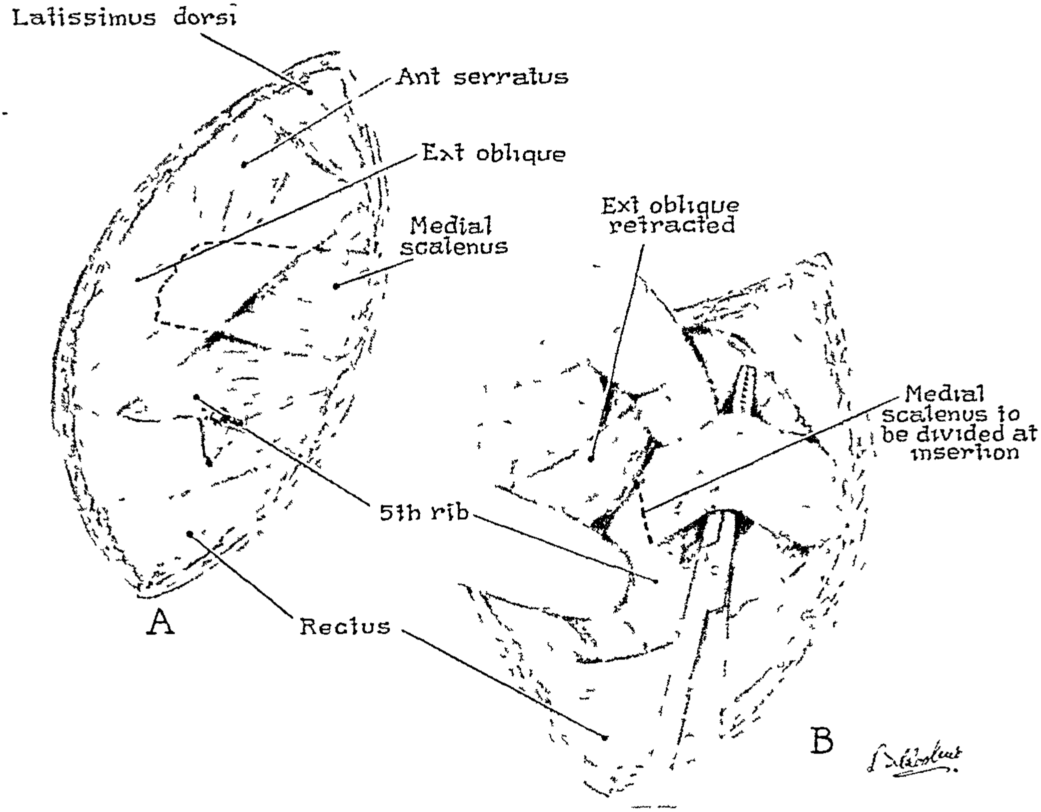

Fig 2.—*A*, Three important landmarks are brought into view the scalenus medius, the serratus anterior, and the external abdominal oblique.

B, The aponeurosis of the medial scalenus is put on stretch with a straight clamp prior to division of its aponeurosis at its insertion onto the fifth rib

A straight clamp is inserted under the scalenus medius and is retracted caudad, lifting the aponeurosis from its rib attachment. The stretched avascular aponeurosis (Fig. 2, *B*) is transected, allowing the scalenus medius to fall cephalad with ease, and exposing the fourth intercostal space. It should be noted that exposure to the intercostal muscles is achieved completely by muscle retraction. Neither the latissimus dorsi, the external oblique, the serratus anterior, nor the scalenus medius need be transected. In order to avoid bloody transection of the intercostals, the full jaw length of a straight clamp is first inserted under the fibers of the external intercostal muscle midway in the intercostal space The muscle fibers are than separated by either incision between the clamp jaws, or by gentle traction of the clamp toward the skin (Fig 3, *A*). The internal intercostal muscle is similarly divided.

The parietal pleura is now visualized During the expiratory phase of respiration, the pleura is opened The fourth and fifth ribs are then separated by the gradual opening *of a self-retaining retractor At this point, the digi*tations of the serratus anterior are seen as thick muscle bundles straddling the intercostal space in the upper portion of the wound, the rectus abdominus is identified traversing the lower aspect of the wound If necessary these muscles may be split in the direction of their fibers to obtain greater exposure.

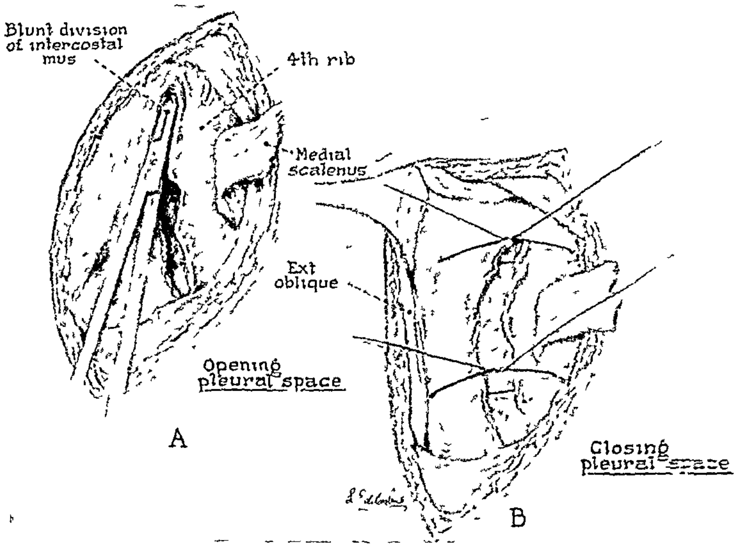

Fig 3 —A, The intercostal muscles are divided midway in the fourth interspace
B, Closure of the thoracotomy is begun by approximating the fourth and fifth ribs with *two pericostal silk sutures*

THE CLOSURE

muscle is now reapproximated to the subcutaneous fascia (Fig. 4, *B*), preferably with interrupted silk sutures. (4) The subcutaneous tissue, and (5) the skin are closed in layers. A rubber catheter can be placed in the pleural space and brought out through the wound in order to allow aspiration of air. The catheter is removed before the final suture is set in place.

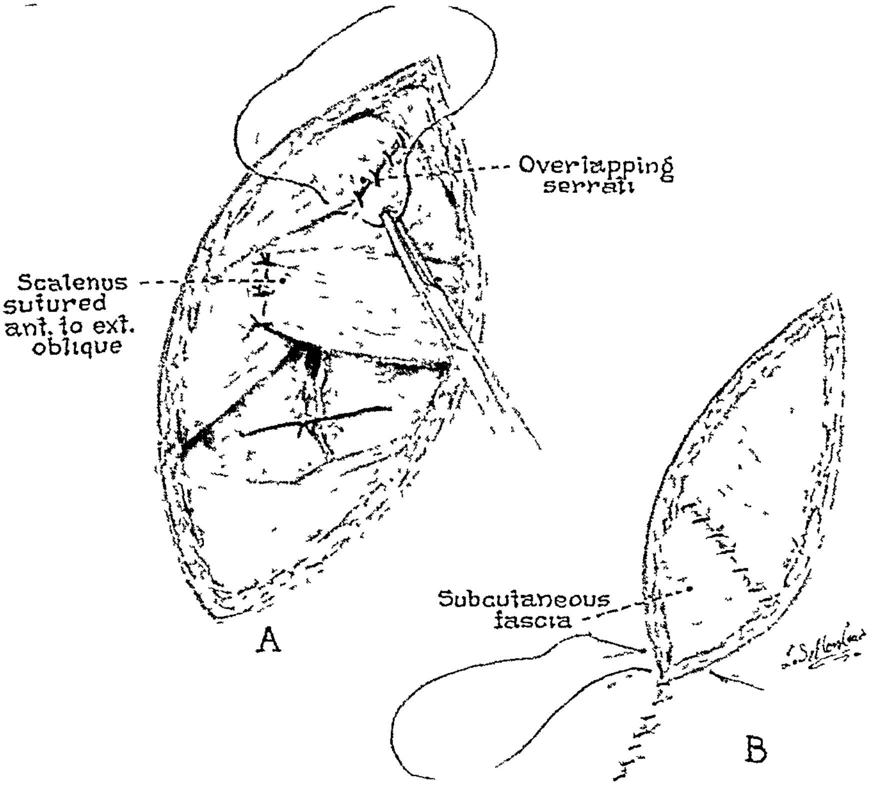

Fig. 4.—*A*, The thick bundles of the serratus anterior overriding the fourth interspace are reapproximated. The scalenus medius is sutured to the antero-superior margin of the external abdominal oblique.

B, The latissimus dorsi is reapproximated to the subcutaneous fascia. The subcutaneous tissue and skin are closed.

DISCUSSION

In other laboratories, the latissimus and longissimus dorsi, the scalenus, the serratus anterior, the external abdominal oblique, and the rectus abdominus are variously incised. Many operators routinely employ subperiosteal rib resection.[2, 3] It is our experience that in the large majority of experimental chest procedures such extensive surgery is unnecessary; it adds to the operating time; it entails significant blood loss and trauma; it involves the use of large amounts of foreign body silk; and it makes the closure less secure.

In over 150 dog operations, this new technique has been used without a single wound complication. The operating time usually does not exceed 3 minutes for the thoracotomy and 6 minutes for the closure. There is usually no bleeding except in the incision of the skin and subcutaneous fat, and little or no silk is needed for hemostasis below this level.

SUMMARY

Major emphasis is placed upon careful technique and a thorough understanding of the anatomy as prerequisites to good thoracic surgery in the experimental animal In the canine the absence of the clavicle alters the structural relationships of a number of muscular and ligamentous attachments, particularly that of the scalenus medius which becomes an important landmark in the thoracotomy

With this anatomy in mind a new technique for thoracotomy is developed in which retraction of muscle and fascia is the predominant feature The latissimus dorsi and the scalenus medius are separated from their local fascial and aponeurotic attachments These muscles and the adjacent serratus anterior and rectus abdominus are then retracted to allow wide exposure to the intercostal space without rib resection Thus transection of all major muscles is completely avoided Because of the careful thoracotomy the closure is made a simple and secure procedure of reapproximation

This new approach has been employed in over 150 cardiac experiments without a single wound complication The method has proved to be quick and easy, avoiding unnecessary blood loss and trauma and ultimately facilitating the post operative recovery

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A STUDY OF DIAPHRAGMATIC AND CRURAL INNERVATION BY THE DIRECT RECORDING OF ACTION POTENTIALS IN THE DOG

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INTRODUCTION

SURGERY for hiatus hernia and its related problems has attracted interest in the innervation of the diaphragm and its component parts surrounding the esophagus. Collis and his associates[1] have suggested that in performing reparative surgery of hiatal hernias, the nerve supply to the left crus may be interrupted. His interest in this problem stimulated him and his co-workers to make a thorough anatomic study of the nerve supply to this region of the body.[2] According to this work, the right crus was invariably innervated by the right phrenic nerve and the left crus by the left phrenic nerve. Botha[3] extended these studies to include a variety of animals, including the dog, and found no evidence of contralateral crural innervation either by anatomic technique or following phrenic nerve stimulation. Ogawa and co-workers,[4] however, recently described crossed innervation of the dogs' right crus in approximately 30 per cent of the animals studied.

Because the difficulties of visually tracing fine nerve twigs from origin to termination are considerable, a physiologic approach to the problem of crural innervation was thought to have certain advantages. In the present study, the criterion of innervation was an action potential picked up from crura or diaphragms when either phrenic nerve was stimulated by single electrical pulses.

METHOD

Eleven mongrel dogs were anesthetized with Nembutal and intubated. A Pneophore* demand-type respirator was attached to the endotracheal tube to provide ventilation after the thorax was opened. A midline incision was made from just below the umbilicus to the sternal notch and the sternum was split

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*The Mines Safety Appliance Co., Pittsburgh, Pa.

in the midline. Both phrenic nerves were dissected from the mediastinum. The liver was then removed as described by LeVeen and Lewis[5] and a plastic (Tygon) cannula with an attached side arm was interposed between the superior and inferior caval veins. The portal vein was then attached to the side arm. This system allowed restoration of caval flow from the inferior vena cava and portal system (Fig. 1). The animal was immediately heparinized. With the removal of the liver, the crura could be clearly visualized. Plastic electrodes with imbedded silver wire contact points were then accurately attached by fine suture to each crus and each diaphragmatic leaf (Fig. 1). Contact points of these recording electrodes were 0.5 mm. in diameter and 3 mm. apart. The previously mobilized phrenic nerves were sectioned 4 inches from their termination and the distal ends passed through stimulating electrodes. A variable frequency stimulator was used for stimulating nerves and a 4-channel direct recorder for recording action potentials. With this arrangement, action potentials could be recorded simultaneously from both diaphragmatic leaves and both crura. The phrenic nerves were stimulated by single pulses.

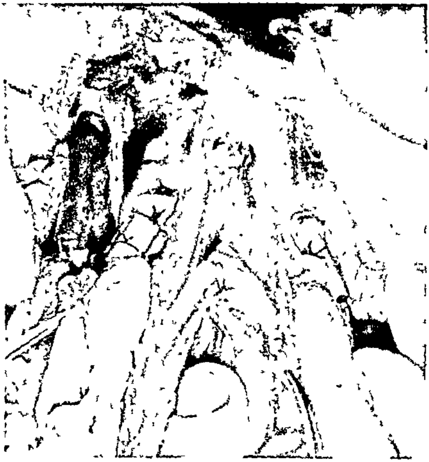

Fig 1.—Photograph of crural electrodes in position The animal's chest is located superiorly, the abdomen inferiorly. The cut edge of the diaphragm extends diagonally across the upper part of the field. The liver has been removed Each electrode is on crural muscle. The esophagus lies between the crura To the right of the dog's right crus is the cannula retaining continuity of the inferior vena cava and portal vein

RESULTS

In each of the 11 animals, action potentials were recorded from the right diaphragm and right crus when the right phrenic nerve was stimulated, and from the left diaphragm and left crus when the left phrenic nerve was stimulated (Table I, Fig. 2). In 4 animals, action potentials were also recorded from the right crus when the left or contralateral phrenic nerve was stimulated. There was no instance in which action potentials from the left crus followed stimulation of the right phrenic nerve. Thus, although the left crus was only innervated by the ipsilateral nerve, it was not unusual for the right crus to be innervated by both phrenic nerves.

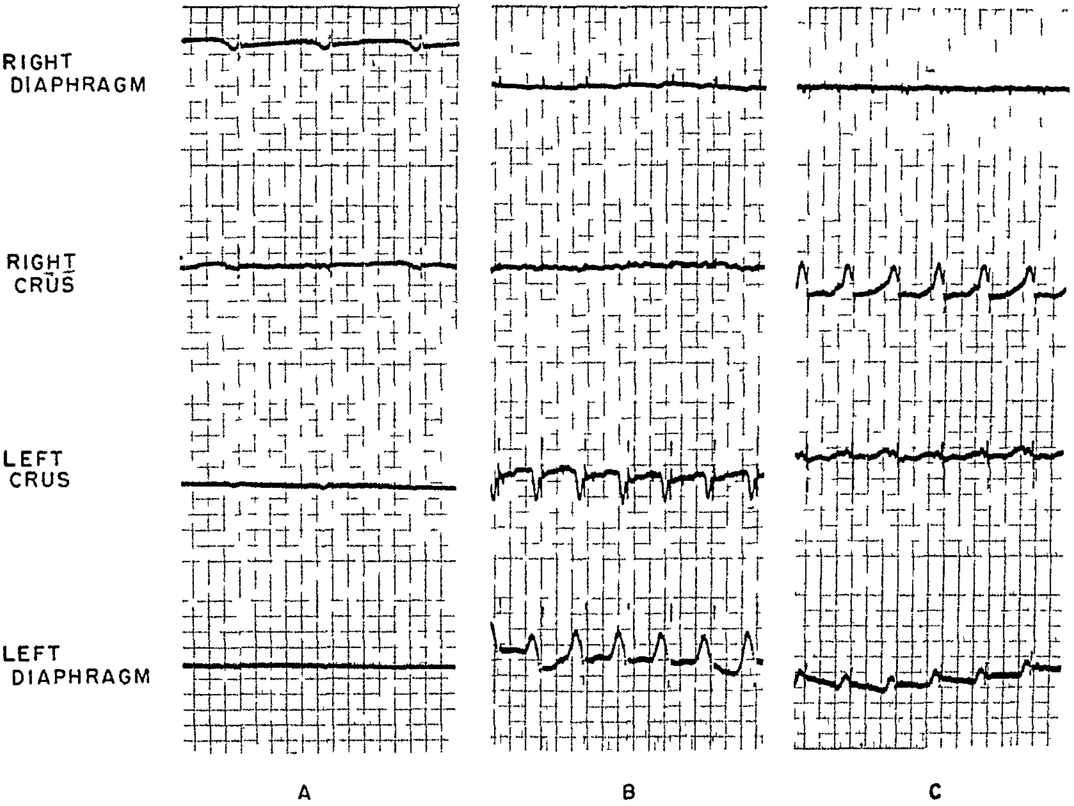

Fig. 2.—Action potentials recorded from crura and diaphragm when right (*A*) and left (*B* and *C*) phrenic nerves were stimulated by single pulses. Records *A* and *B* illustrate ipsilateral innervation only. Record *C* shows crossed innervation of the right crus by the left phrenic nerve.

TABLE I

EXPERIMENT	STIMULATION OF RIGHT PHRENIC NERVE ACTION POTENTIALS FROM				STIMULATION OF LEFT PHRENIC NERVE ACTION POTENTIALS FROM			
	RD	RC	LD	LC	RD	RC	LD	LC
3/29/57	+	+	+*	–	–	+	+	+
5/ 8/57	+	+	–	–	–	+	+	+
5/20/57	+	+	–	–	–	–	+	+
6/24/57	+	+	–	–	–	–	+	+
7/12/57	+	+	+*	–	+*	–	+	+
9/13/57	+	+	+*	–	–	+	+	+
9/27/57	+	+	–	–	–	–	+	+
11/ 1/57	+	+	–	–	–	–	+	+
11/ 8/57	+	+	–	–	+*	–	+	+
11/15/57	+	+	–	–	–	+	+	+
12/ 5/57	+	+	–	–	–	–	+	+

*Recording electrode on diaphragm contralateral to nerve stimulated was near the midline.

+ = Action potentials present; – = Action potentials absent. RD = Right diaphragm, RC = Right crus, LD = Left diaphragm; LC = Left crus.

DISCUSSION

These results are at variance with those previously published in that the muscle mass to the right of the esophagus was commonly innervated by both phrenic nerves This difference with observations of others is perhaps not surprising, for the difficulties of the physiologic methods employed would appear fewer than those one must encounter in tracing nerve fibers down to their terminals in postmortem material This finding is possibly all the more surprising because the inner margins of the esophageal hiatus are usually made up on both right and left by muscle bands which form the right crus, i e, which insert to the right of the midline One might assume, therefore, that branches of the right phrenic nerve would also pass to both sides of the esophagus and innervate the muscle adjacent to the esophagus This, however, must be uncommon as compared to the types of innervation described in this and in the anatomic studies To our knowledge, no instance has been described in which muscles to the left of the esophagus have been innervated by the right phrenic nerve

The innervation and structure of the diaphragm have been recently reviewed by Botha[3] and by Ogawa[4] to whom the interested reader is referred It may be observed in passing, however, that there are considerable variations in the position of the esophageal hiatus and in the origin and destination of the muscles which surround it Some of these variations are doubtless predispositions to herniation It is perhaps difficult to conceive that, where there is so much variability of structure, there should be the uniformity of innervation previously suggested

CONCLUSIONS

1 Innervation of the diaphragmatic crura was studied in 11 hepatectomized dogs by recording muscle action potentials from crura and diaphragms following phrenic nerve stimulation

2 An action potential was always recorded from the diaphragm and corresponding crus when the ipsilateral phrenic nerve was stimulated

3 In 4 of the dogs, the right crus was innervated also by the left or contralateral phrenic nerve There was no instance in which the left crus was innervated by the right phrenic nerve

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EXPERIMENTAL USE OF NYLON MESH-SUPPORTED PERICARDIAL GRAFTS FOR CLOSURE OF FULL-THICKNESS ESOPHAGEAL DEFECTS

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THE availability in recent years of an increasing number of synthetic plastics which are well tolerated by the human body has stimulated considerable interest in the suitability of these materials for the support and replacement of certain anatomic structures. The success of synthetic vascular substitutes in arterial replacement and bypass and that of plastic meshes in the repair of hernial defects is well known.

The use of synthetic materials in esophageal surgery has been directed largely toward the use of impervious tubes for the replacement of resected segments of esophagus.[4, 1] There has been little interest in the usefulness of permeable plastics in esophageal surgery. The suitability of nylon mesh for the replacement of resected portions of esophageal musculature and the adequacy of its tolerance in this area has been reported recently by the authors.[6] In addition, the senior author[7] also has recorded the successful clinical use of a patch of nylon mesh for the support of a section of markedly weakened esophageal wall, following extramucosal resection of an obstructing subcarinal mediastinal granuloma. Only a tissue-paper thin mucosal remnant covered the esophageal lumen in the area of this resection.

While it is quite apparent that a permeable plastic such as nylon mesh could not be used alone for the closure of full-thickness esophageal defects, the experiences cited above have led us to investigate the feasibility of combining the use of nylon mesh for support and some nearby, relatively strong autogenous tissue for permanent or temporary water-tight closure of the defect. Pericardium was selected because of its availability and strength. The successful use of nylon net-supported tubes of autogenous pericardium in the experimental replacement of resected segments of thoracic aorta was described by Adler[2] in 1955. The combined use of nylon mesh and pericardium in esophageal surgery has not, to the authors' knowledge, been reported.

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MATERIAL AND METHODS

Healthy mongrel dogs were used. An effort was made to limit the oral intake of liquids and solid food for a short period prior to operation. Intravenous Pentothal was employed for anesthesia. Oxygen was administered through an endotracheal tube by means of a mechanical respirator. The lower left pleural cavity was entered through an intercostal incision. The lower esophagus was mobilized and secured between Potts coarctation clamps. An oval full thickness defect of standard size measuring approximately 2.5 by 2 cm., was made by resecting a segment of esophageal wall (Fig. 1). The Potts coarctation clamps were useful not only in manipulation of the esophagus but also in the control of bleeding along the margins of the defect during graft placement and in prevention of possible contamination of the pleural cavity and the area of operation by gastric and upper esophageal contents.

A free pericardial graft was obtained by resecting a portion of the adjacent pericardium and tailoring it to the approximate size of the defect. The graft was secured to the margins of the defect with interrupted sutures of 5-0 arterial silk through the relatively thick and tough mucosal layer. Eight such anchoring sutures generally were employed. A continuous circumferential suture of 5-0 arterial silk then was used in an attempt to achieve a water-tight union between the pericardial graft and the mucosal layer at the margins of the defect. A piece of fine mesh nylon, of a type already shown to be tolerated well in the wall of the esophagus, was cut to the approximate size and shape of the defect. The nylon mesh fabric (241 F)* contained 270 by 204 threads per square inch. This supporting nylon mesh was secured to both esophageal mucosa and muscle layers at the margins of the defect with interrupted sutures of 5-0 arterial silk. The left thoracotomy incision was closed in layers and a catheter, left in place during the closure, was aspirated and withdrawn.

In a few animals, the use of the supporting nylon mesh was omitted so that these animals might serve as controls. In one animal, only nylon mesh was used to cover the defect.

The animals were given nothing by mouth for the first 24 hours after operation. On occasion intravenous fluids were given during this period. For the following 10 days they were given only milk by mouth. A soft meat diet then was given for one month prior to the resumption of a regular diet. Intramuscular penicillin, 200,000 units a day, was given for the first 5 days after operation.

RESULTS

The 6 control animals in which a free pericardial graft was employed for water-tight esophageal defect closure without supporting nylon mesh all died 3 and 4 days following operation. In all 6 death was found to be due to perforation of the graft with gross contamination of the left pleural cavity. The one animal in which only nylon mesh was used for defect closure died of empyema 5 days after operation.

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*Nylon fabric was obtained from Stehli Company, Inc., 1372 Broadway, New York City.

A nylon mesh-supported free pericardial graft was used as described for closure of a standard full-thickness esophageal defect in 24 consecutive animals. Satisfactory defect closure with survival of the animal and no postmortem evidence of empyema was achieved in 21 of the 24. Three dogs died in 3, 5, and 6 days following operation, with empyema and evidence of disruption of the graft closure.

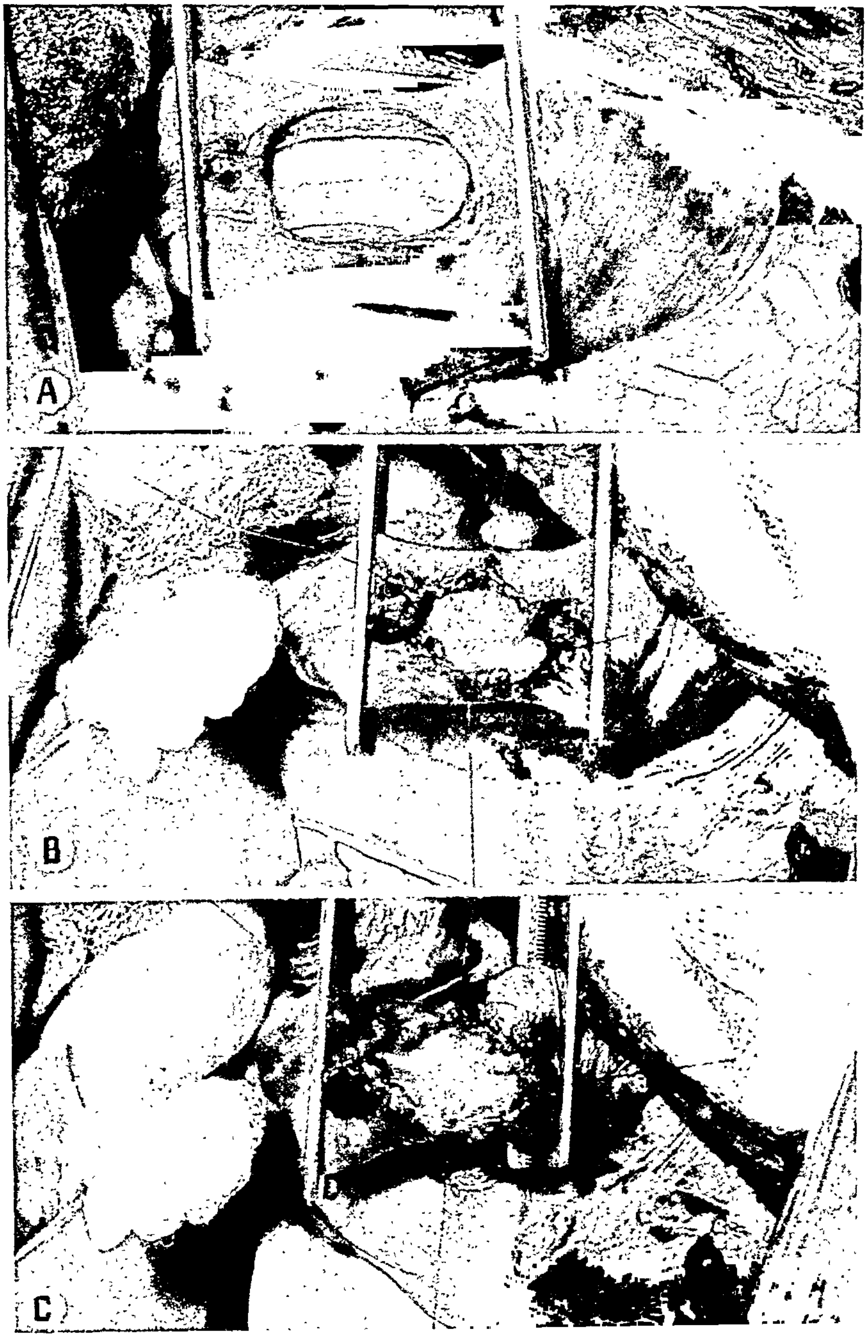

Fig. 1.—Photographs at the time of operation showing the standard full-thickness esophageal defect employed (*A*) before and (*B*) after closure with a free pericardial graft. Reinforcement of the free pericardial graft with fine mesh nylon is pictured in *C*.

The fate of the free pericardial graft and the supporting nylon mesh in surviving animals was of interest. The fate of these materials gave some insight into the pattern of esophageal defect healing. Animals were examined at autopsy at varying periods of time following operation in order to evaluate the integrity of the defect closure and to study the pattern of defect healing (Table 1). The defect closure of pericardium and supporting nylon remained relatively intact until about 14 days after operation. At this point, the pericardial graft tended to disappear, apparently sloughed into the lumen of the esophagus, and progressive defect contracture with ballooning of the nylon mesh patch into the lumen of the esophagus generally continued from 2 weeks to 2 months (Fig. 2). In 5 of the 7 animals examined more than 60 days after operation, the nylon mesh was no longer present and was presumed to have been discharged into the esophageal lumen. It was gone in all of 3 animals examined more than 80 days after operation. Although some thinning of the wall of the esophagus was noted

TABLE I. SUMMARY OF POSTMORTEM FINDINGS IN THE 21 ANIMALS WITH SUCCESSFUL DEFECT CLOSURE

DOG NO	INTERVAL FROM OPERATION TO AUTOPSY (DAYS)	STATUS OF GRAFT AND DEFECT AREA AT AUTOPSY
700	8	Graft intact with nylon in place, no defect contracture good closure
658	9	Graft intact with nylon in place, no defect contracture no leak
657	10	Graft intact with nylon in place, no defect contracture satisfactory closure
662	11	Graft intact with nylon in place, no leak or defect contracture
708	14	Graft intact, no contracture, nylon in place
665	16	Nylon loose in one area, defect closure adequate
710	20	Defect contracture, nylon starting to balloon into lumen of esophagus
711	21	Defect contracture, nylon ballooning into lumen, suture becoming free in one area
701	27	Defect contracture, nylon partially free and ballooning into lumen
705	27	Defect contracture, nylon ballooning into lumen
706	27	Defect contracture, nylon ballooning into lumen
690	52	Defect contracture, nylon ballooning into lumen and becoming detached
688	55	Defect contracture, nylon ballooning into lumen
689	60	Defect contracture, nylon ballooning into lumen
677	63	Nylon gone, some thinning of esophageal wall in area of contracted defect, defect closed by ingrowth of fibrous connective tissue
692	68	Nylon gone, defect contracted and closed by ingrowth of adjacent connective tissue
666	76	Defect contracture, nylon ballooning into lumen
660	77	Defect contracture nylon ballooning into lumen and partially detached
667	89	Nylon gone, some granulation tissue projecting slightly into lumen in area of contracted defect
656	137	Nylon gone, defect contracted and closed by ingrowth of adjacent connective tissue
638	161	Nylon gone, defect contracted and closed by ingrowth of adjacent connective tissue, some thinning of esophageal wall in area of contracted defect

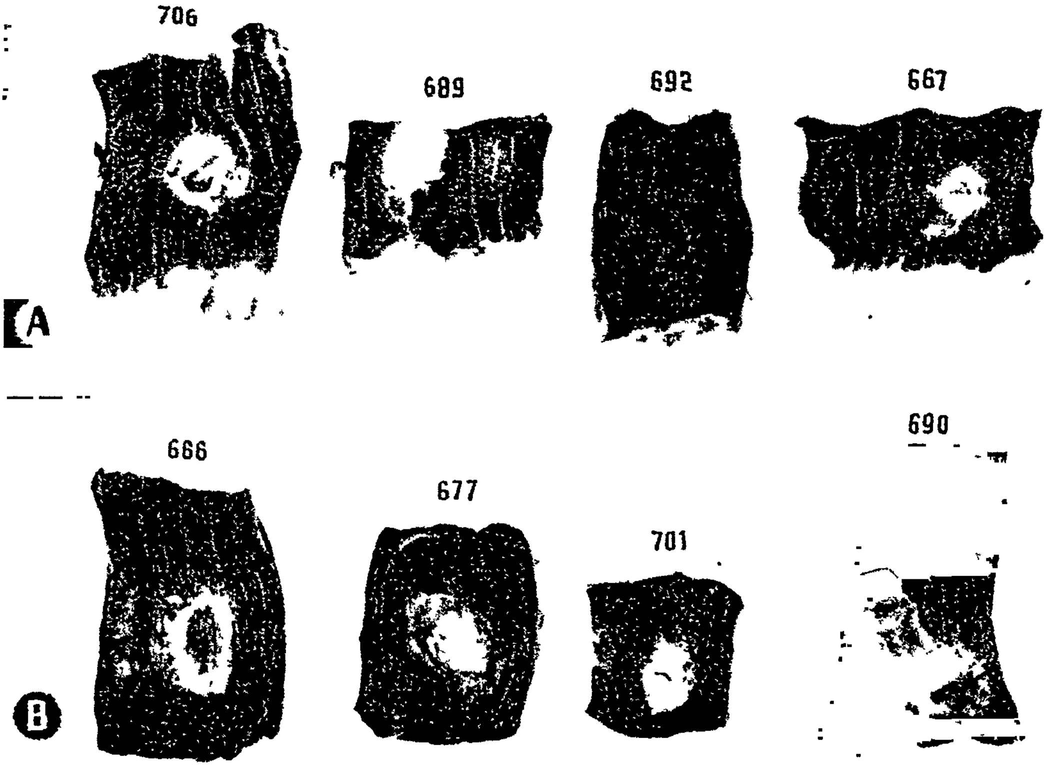

Fig 2 —Photograph showing the appearance of the esophageal defect closure area from the lumen of the esophagus in 8 animals, on postmortem examination at varying periods following operation In some, the nylon mesh has become partially detached or is ballooning into the lumen; in others it has disappeared More detailed information on the specimens pictured may be obtained from Table I

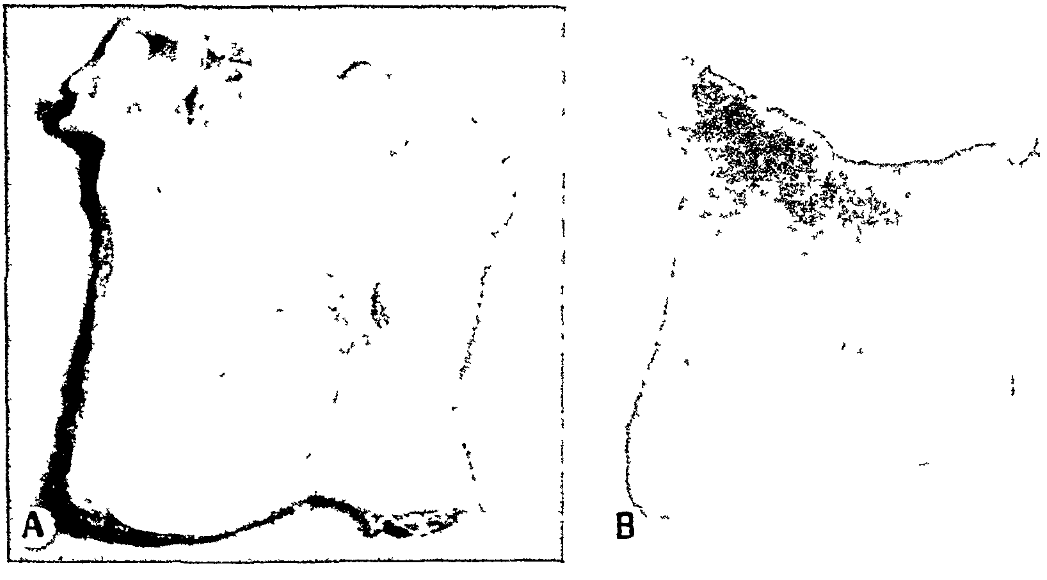

Fig 3 —Photographs of the area of esophageal defect closure in Dog 638 over 5 months after operation The healed area of defect closure may be seen in *A* The thinning of the esophageal wall in the area of defect closure is demonstrated by transillumination in *B*

in the area of defect closure after disappearance of the nylon (Fig 3), no gross evidence of herniation or significant weakness of the esophageal wall in these areas was encountered Furthermore, no contracture of the lumen of the esophagus at the level of the defect closure was found

DISCUSSION

The inadequacy of unsupported free pericardium for the closure of full-thickness esophageal defects of the standard size used in this study was conclusively demonstrated by the death of all 6 animals of graft disruption in this control group, from 3 to 4 days after operation On the other hand, the survival of 21 of 24 dogs with successful defect closure when nylon mesh was added to support the free pericardial graft was regarded as significant evidence of the important role played by the supporting nylon in achieving successful defect closure

When this study was begun, it was hoped that the free pericardial graft would survive and remain intact in the area of defect closure and that the nylon mesh would be incorporated into the newly formed esophageal wall through the ingrowth into its interstices of fibroblasts and blood vessels from surrounding connective tissue This did not prove to be the case The free graft of pericardium appeared to serve merely as a temporary seal until a permanent seal could develop from surrounding connective tissue The pericardial graft generally disappeared in the early days after operation Permanent defect closure was produced by a combination of defect contracture and healing in the area of permanent defect seal from surrounding connective tissue The defect contracture caused a progressive ballooning of nylon mesh patch into the lumen of the esophagus The nylon patch generally became detached from the margins of the contracted defect and disappeared approximately 2 months following operation

Adler[1] in 1956 reported the results of experimental studies in which free grafts of pericardium were used for the support of purposely faulty end to end esophageal anastomoses The pericardial graft was secured to the esophagus in the area to be protected with a thrombin fibrinogen coagulum He found that the free pericardial graft secured in this manner protected the faulty anastomoses in 5 of 10 dogs Only 2 of 10 dogs with unprotected faulty anastomoses survived and one of these dogs developed a localized abscess

The greater success of nylon mesh supported pericardial grafts, as experienced in this study, would appear to suggest that this method of closure of esophageal defects of limited size and of reinforcement for questionable esophageal anastomoses is worthy of a clinical trial

SUMMARY

The experimental use of nylon mesh supported free pericardial grafts for the closure of relatively large full thickness esophageal defects of standard size is reported The operation was carried out as described in 24 dogs Twenty one of the animals survived with successful defect closure All of 6 dogs in

which only a free pericardial graft was used to cover the defect died of graft disruption and gross pleural contamination 3 and 4 days after operation. The pattern of defect healing is described and possible clinical application of these observations is discussed.

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FOREIGN BODY BRONCHOESOPHAGEAL FISTULA*

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BRONCHOESOPHAGEAL fistulas due to esophageal foreign bodies are seldom reported A review of the medical literature through 1957 yielded only 16 cases, 11 of which were concentrated in the doctorate thesis of Criot published in 1898 at Lyons, France Coleman and Bunch[1] in a collective review of the literature through 1950 added 4 cases, one, however, due to tracheal rather than esophageal foreign body In 1957, 2 additional cases were reported by Pouyanne and his associates[3] and Lemariey,[2] both occurring in nursing infants

Typically, the symptoms are the same as for congenital tracheoesophageal fistulas, with the addition of a history of esophageal foreign body ingestion The classic symptom is *severe cough following the swallowing of liquid or occasionally of solid food* This cough can sometimes be controlled by positioning the patient while swallowing The appearance of râles in one or both lung fields following the ingestion of liquids (sign of Ono) is described as pathognomonic of tracheoesophageal communication Persistent abdominal distention is common due to the continuous passage of air from the tracheobronchial tree into the esophagus Frequently atelectasis and pneumonia occur if the fistula has been present for any length of time

Unfortunately, as demonstrated in our case, any of the symptoms, except the pulmonary complications, may be absent or so minimal that they are completely overshadowed by the pulmonary findings This is particularly true when the foreign body is nonopaque and no history of ingestion obtained

CASE REPORT

J B No 294779, a 2 year old white female, had been followed in the Pediatric Clinic for approximately one year for asthma and recurrent respiratory infections Acutely ill, with left lower lobe "pneumonia" and a left pleural effusion, she was admitted to the Pediatric Service on June 25, 1958 Thoracentesis yielded a serosanguineous fluid Culture and cell

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*This paper represents the personal viewpoint of the author and is not to be construed as a statement of official Air Force policy

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***Chief Pediatric Service USAF Hospital Lackland AFB Texas blocks were negative. Repeated x-ray studies revealed left lower lobe atelectasis, and bronchoscopy was performed. The left main-stem bronchus and the lower lobe bronchus were edematous, and injected. Serosanguineous fluid was aspirated from the bronchus, and a beta hemolytic streptococcus was cultured. The effusion and pneumonia cleared rapidly on treatment with penicillin. The left lower lobe atelectasis persisted, but finally improved on positive pressure breathing with Alevaire and Isuprel. The patient was discharged after 28 days. Intermittent positive pressure therapy was continued on an outpatient basis. The patient was asymptomatic on this regimen for one month. During a routine weekly check in the Pediatric Clinic, the patient was found to have a recurrence of the complete atelectasis of the left lung. She was immediately readmitted on Aug. 22, 1958.

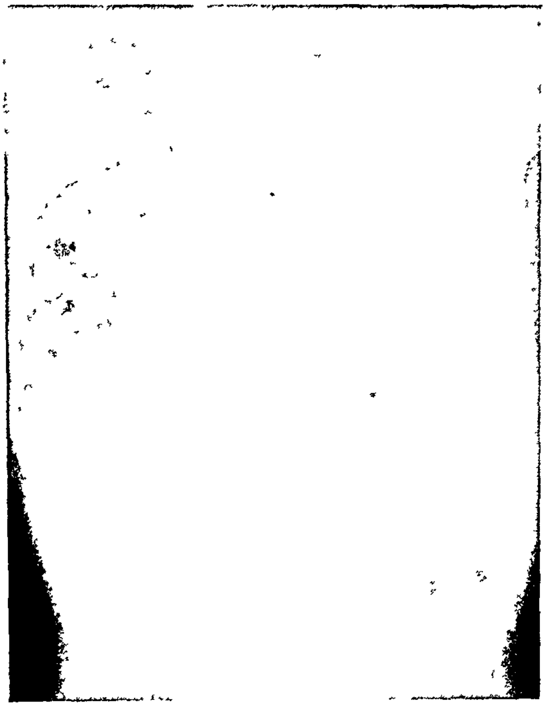

Fig. 1.

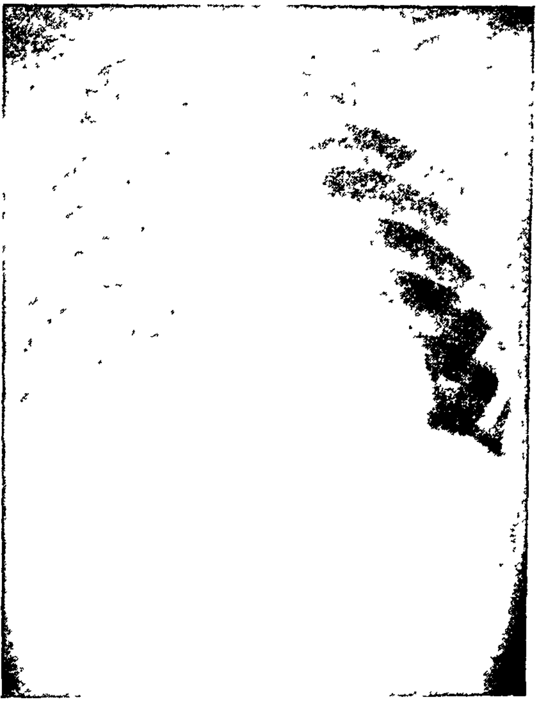

Fig. 2.

Fig. 1.—Chest roentgenogram at time of first admission showing left pleural effusion.

Fig. 2.—Chest roentgenogram at time of discharge from first admission showing completely clear left chest.

The patient was not clinically ill. The positive physical signs were limited to the chest and revealed a respiratory lag on the left with diminished breath sounds. Complete blood count and urinalysis were within normal limits. Stool examinations revealed normal trypsin digestion.

The patient underwent bronchoscopy immediately after admission. The examination was unsatisfactory due to mechanical difficulties. She was placed in moist oxygen with Isuprel and Alevaire. On the following day, x-ray studies revealed almost complete clearing of the atelectasis. Twelve days later chest roentgenograms again revealed complete left lower lobe collapse and bronchoscopy was again performed. Considerable secretions were aspirated from the main-stem bronchus. The upper lobe orifice was patent. Just below the upper lobe take-off, the bronchus was obstructed by a reddish friable mass which was removed by biopsy forceps. The lower lobe bronchus was then aspirated and noted to exchange air adequately. Prophylactic tracheotomy was performed. The pathologic report of the biopsy specimen was granulation tissue consistent with foreign body reaction. The patient's clinical condition began to deteriorate. Gradually she became more apathetic and depressed. The temperature rose daily to 102° F and penicillin therapy was supplemented by Chloromycetin and erythromycin. Serial chest roentgenograms revealed varying degrees of aeration of the left lower lobe despite the septic course.

On Sept 24, 1958 (20 days after bronchoscopy), a left lower lobe lobectomy was performed. A nonopaque foreign body of the bronchus was considered the most likely etiologic agent and in view of x-ray evidence of possible abscess formation and progressive deterioration of the patient despite massive antibiotics, operation was advised.

The operation was carried out under hypothermia with reduction of body temperature to 99° R. At operation, the left lower lobe was completely consolidated and massive inflammatory adenopathy was present in the hilum. On sectioning the bronchus, a copious amount of thick purulent secretion was aspirated from both the main stem and upper lobe bronchi. The upper lobe expanded well after this. The patient withstood the operation amazingly well. The specimen grossly had a peculiar polypoid appearance and a tentative frozen section diagnosis of papillomata of the bronchus was made.

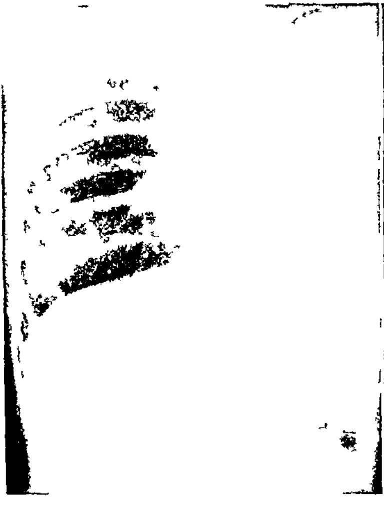

Fig 3

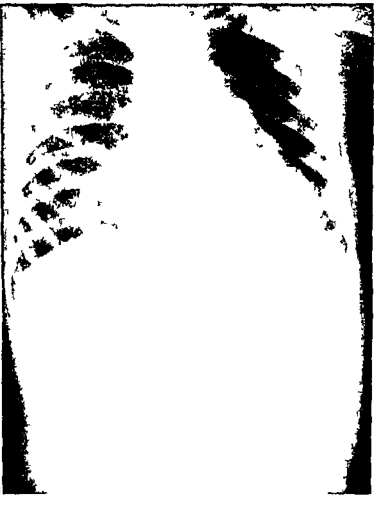

Fig 4

Fig. 3.—Chest roentgenogram on second admission showing total atelectasis of left lung.
Fig. 4.—Chest roentgenogram immediately preoperative showing residual left lower lobe atelectasis and possible abscess.

Hypothermia was maintained for 24 hours postoperatively and then discontinued. The patient did well until noon of the second postoperative day when she exhibited severe respiratory distress and a temperature of 104° F. Abdominal distention was first noted at this time. Intratracheal and gastric suction were employed with some relief of symptoms. The patient appeared to be improving when she suddenly became cyanotic, gasped for breath, and died.

The pertinent autopsy findings were limited to the chest. The right lung was expanded, crepitant, and normal. The left pleural space contained a minimal amount of fluid. The left upper lobe was expanded, but indurated. The entire thoracic contents were removed en bloc. The esophagus was opened longitudinally, and in the middle one third there was a 2 by 2 cm plastic foreign body wedged across the lumen. The edges were sharp and irregular. One corner of the foreign body extended through a slit like fistula, 0.5 cm. in length, which communicated with the left main stem bronchus at the level of the upper lobe orifice. The fistulous tract was fibrous and epithelized. The lobectomy stump was well sealed. The remainder of the autopsy was within normal limits

Following autopsy, a careful search of old outpatient records, and detailed questioning of the parents, revealed that the patient had swallowed a plastic covered button from her mother's nurse uniform in April, 1957 (18 months prior to surgery). She regurgitated the button 5 days after ingestion and was apparently normal. No other history of foreign body ingestion could be obtained

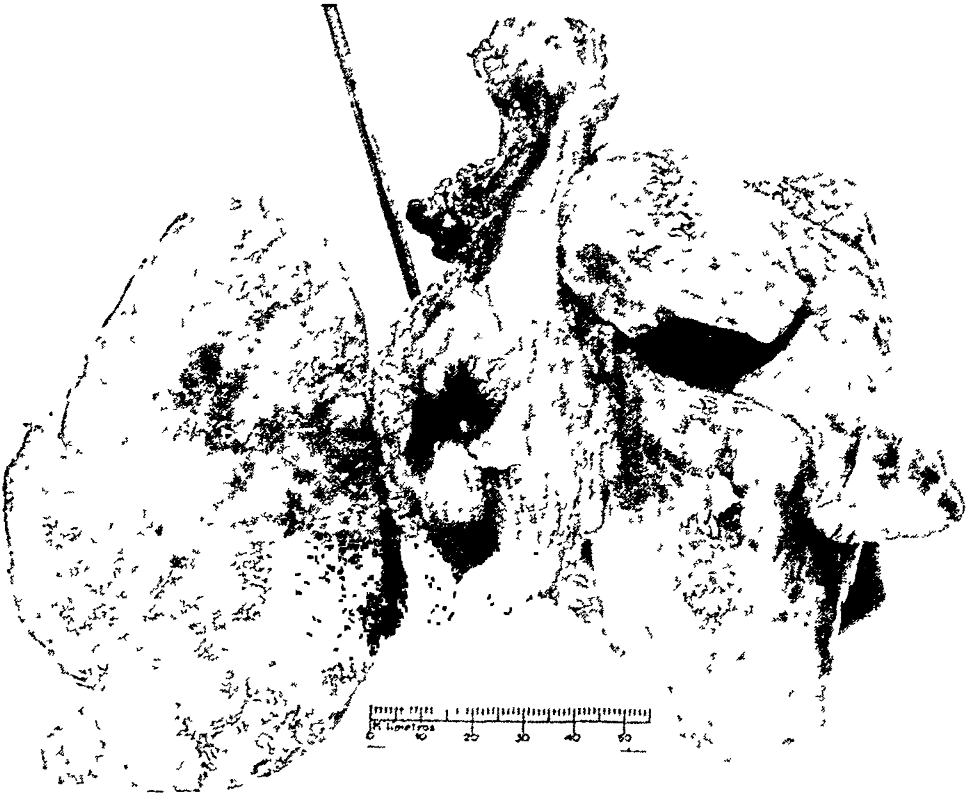

Fig 5.—Autopsy specimen viewed posteriorly showing foreign body in esophagus A metal probe has been inserted through the fistula

DISCUSSION

This case illustrates the vague or practically nonexistent symptomatology that may be presented by a bronchoesophageal fistula secondary to a retained esophageal foreign body. The only symptoms noted during the 18-month period were two transient episodes of wheezing ascribed to asthma. Never was there x-ray evidence to suggest the presence of a foreign body. However, in retrospect, the entire clinical course becomes logical One can only suppose that the plastic covering of the button became wedged in the esophagus in April, 1957, and that the patient regurgitated only the metal frame 5 days later, a fact not noted by the parents. Six months later a diagnosis of asthma was made because of wheezing.

It is easy, in retrospect, to visualize the irritative process that produced the wheezes For a period of over a year, episodes of respiratory infection increased in number, followed finally by pneumonia and atelectasis as the fistula increased in size The most confusing part of the picture was the absence of strangulation symptoms on liquid ingestion We feel that this was due to the impaction of the foreign body in the fistula which prevented the dumping of swallowed fluids into the tracheobronchial tree

One wonders how the diagnosis could have been made antemortem The occurrence of "asthma" in a young child previously free of allergic symptoms certainly should suggest the possibility of foreign body ingestion Critical review of the case has failed to reveal any symptoms which would have indicated the diagnosis At the time of lobectomy, the fistula was above the level of bronchial amputation and not visualized At bronchoscopies, it was obscured by edema, granulation tissue, and by the fact that the foreign body did not actually protrude into the bronchus The only means, other than esophagoscopy, by which diagnosis could possibly have been made would have been by means of a Lipiodol swallow

SUMMARY

A case of bronchoesophageal fistula due to ingestion of foreign body is reported with a review of 16 cases from world literature Foreign body ingestion must be considered when signs of asthma appear in a previously allergy free patient Examination of the esophagus should be considered in cases of unexplained recurrent pneumonia and atelectasis

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AN ELECTRICALLY CONDUCTIVE CARDIAC SUTURE

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The necessity for applying an artificial stimulus to the heart to evoke effective ventricular contractions arises occasionally. This problem is of increasing frequency of occurrence, in part due to the development of "open-heart" surgery with its incidence of surgical interruption of the conduction system. Usually these incidences occur at critical times, and the patient's survival depends on the efficacy of the artificially stimulated contractions.

This résumé is confined to the discussion of those syndromes in which ventricular myocardial contractility is adequate and the primary defect is the absence of a stimulus of sufficient frequency and or/intensity.

An intermittent electrical impulse is the most reliable type of artificial stimulus. Several "pacemakers" are commercially available. The electrodes can be applied externally at two points on the chest wall and the stimulus increased in intensity until a perceptible pulse, synchronous with the pacemaker rhythm, indicates that the ventricles are responding.

Electrodes can be applied internally via a thoracotomy incision, and the response further evaluated by direct vision.

There are several difficulties. The external electrodes cause spasmodic contractions of all skeletal muscle within their field, as well as myocardial tissue. The resultant artificial clonic local convulsion soon becomes intolerable to the conscious patient, and severely handicaps the observation and examination of the critical patient.

When peripheral vascular hypo- or hypertonia renders pulses imperceptible. the effectiveness of the electrical stimulus is open to question. With a thready pulse and jerking chest musculature, one is never sure (in the closed chest) at what point an increasing intensity is sufficient to stimulate the myocardium.

It is suggested that in medical heart block the contractions be re-established by use of a pacemaker and external electrodes. If tentative cessation of the stimulation results in immediate failure of the circulation, the chest should be opened.

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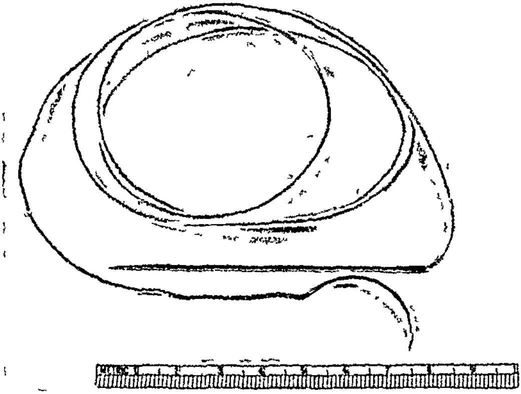

Fig. 1—The electrically conductive suture is commercially available in sterile packets. Silver wire is braided around a silk core. Polyvinyl tubular insulation allows autoclaving.

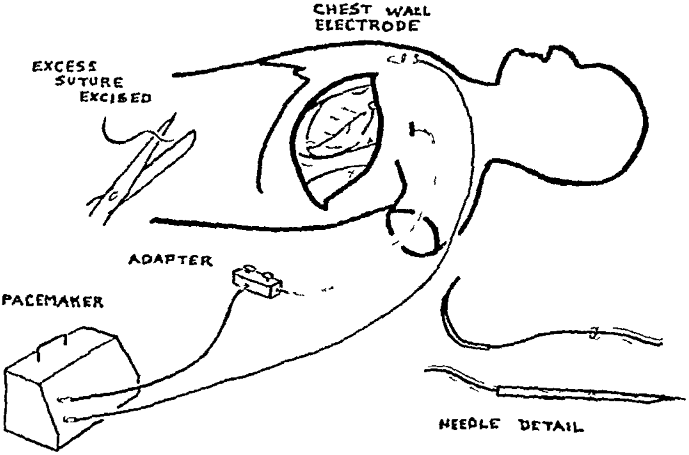

Fig. 2—Use of the electrode wire sutured into the myocardium with a nonspecific external electrode.

An opened chest facilitates evaluation of the heartbeat by direct vision. However, it is axiomatic that the sooner the wound is closed, the better. Closure of the incision while the external electrodes are in operation is clumsy and difficult.

Many of the above problems have been solved by the application of a wire electrode directly into the myocardium. Such an apparatus is now commercially available.* A silver wire is doubly armed with swaged needles, one curved and one straight. The entire wire is insulated with a polyvinyl sheath, except for the 4 inches adjacent to the curved needle The surrounding insulation is swaged into the straight needle. The suture is supplied in sterile packets ready for use.

A single stitch is taken into the ventricular myocardium. The curved needle and the bare wire are pulled through until the polyvinyl insulation encounters the muscle. The needle is then cut off leaving a 1 to 2 cm. length of wire protruding. This can be secured to the myocardium with a 5-0 silk stitch.

A spot on the chest wall is then chosen for the penetration of the straight needle. This should be away from the incisional edges so it will not be dislodged during wound closure. It should be in such a location that the suture, when withdrawn from the chest, will pull out of the heart in the long axis of the wire, and not lacerate the myocardium by sawing action as in a right angle pull-out. The straight needle is attched directly to the pacemaker attachment. Adapters are commercially available* to join all standard pacemakers with the conductive straight needle. The second (nonspecific) elctrode is applied externally to the right of the sternum or, as an alternative, two internal suture electrodes can be utilized.

With such a setup, one can be confident that an effective stimulus is being applied to the myocardium. This assurance should eliminate one variable from the multifaceted problem of sustaining the critically ill patient with heart block.

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*Ohio Chemical Co., Madison, Wis.

THREE USEFUL CLAMPS FOR CARDIOVASCULAR SURGERY

S Abraham Cuadros, M D , Lima, Peru

IT IS CLEAR that cardiovascular surgery has progressed at an ever accelerating rate in the last few years, providing in a short time the answers to a large number of problems which for a long time remained insoluble To keep pace with expanding horizons, continued advances in surgery, and new and perfected techniques, it is necessary to use new and better instruments

One cannot fail to recognize that one of the most ingenious and useful instruments in this field of surgery is the Potts Smith clamp, with its advantages of safety for partial occlusion of the vessel lumen It has, however, the disadvantage that it cannot always be applied as desired, for instance when full mobilization of a vessel is difficult, or when there are important branches at the exact site of the clamping which cannot be divided, and also when it is necessary to apply it rapidly in situations of emergency For these reasons, Blalock introduced an improved modification, yet even this has not proved fully satisfactory

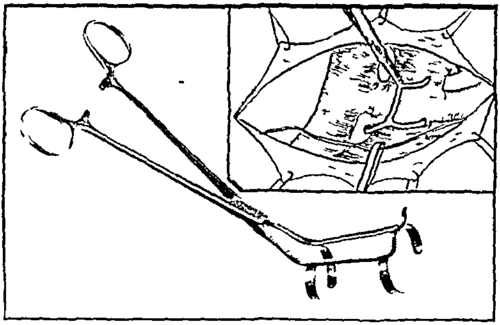

Fig 1 —This figure shows the first clamp and one use of this clamp in an atypical patient ductus arteriosus which is just below the carotid artery

To combat the difficulties just mentioned, two clamps have been devised The first clamp (Fig 1) has two metal arcs on each limb When the clamp is closed these form a circle which embraces the vessel to be occluded With this, one avoids all the disadvantages of the Potts Smith clamp The drawing in Fig 1 illustrates the clamp in use

The clamp seen in Fig 2 has two small rings on each limb This allows a ligature to be passed around the vessel and fixes it safely, giving the clamp

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From the Karolinska Institute Stockholm Sweden
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an extremely simple and effective character, as can be seen in the drawing in Fig. 2.

One of the difficulties often encountered in the clamping of the aorta in its approach is the slipping of the end of the clamp, due to aortic arterial pressure and, in certain circumstances, this can become a serious problem. Having noticed that this slipping is due to weakness of the clamp at its free extremity, it has been found possible to overcome this difficulty with a hinged screw which, when screwed up, effectively prevents the clamp from slipping at its free end. A third clamp, incorporating this hinged screw, can be seen in Fig. 3. The clamp in use is illustrated in the drawing in Fig. 3.

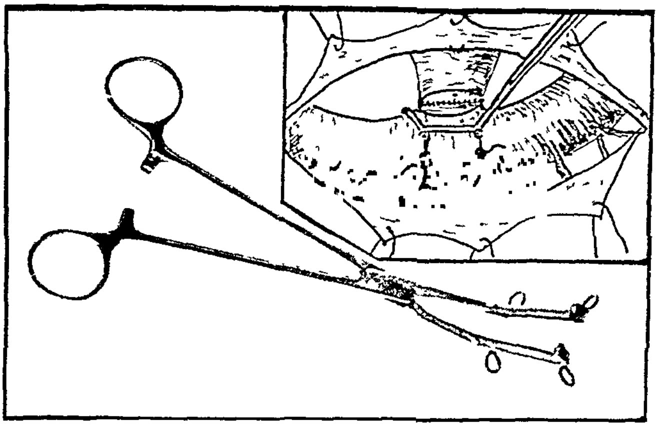

Fig. 2.—This figure shows the second clamp and one use of this clamp in a Potts operation without cutting the branches of the descending aorta.

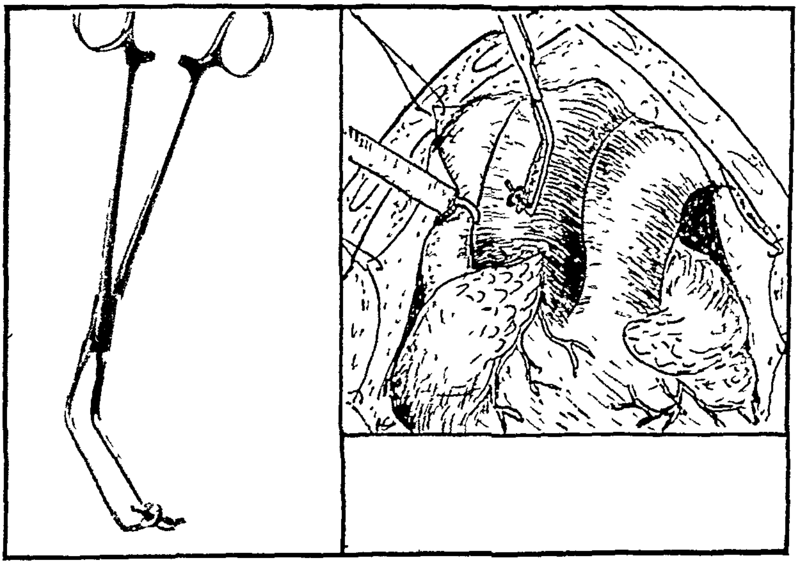

Fig. 3.—This figure shows the third clamp and its use in aortic valvulotomy under direct vision (hypothermia).

I wish to thank Prof. A. L. d'Abreu from the Queen Elizabeth Hospital (University of Birmingham, England) in whose Laboratory of Experimental Surgery these instruments were devised.

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Members Deceased

Duff S. Allen
Daniel C. Elkin
Chevalier Jackson

ANNUAL MEETING NOTES

The Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery was held in Los Angeles, California, April 21, 22 and 23, 1959. There were 801 physicians who registered for the scientific sessions. In addition there were 87 wives present.

The American Association for Thoracic Surgery has been granted three seats for representatives on the Board of Governors of the American College of Surgeons. These representatives were announced as Drs. George H. Humphreys, II, Edward M. Kent, and Paul C. Samson serving a one, two and three year term respectively. Each year the recurring vacancy will be filled by an Active or Senior member of the AATS who will then serve a regular three year term.

The following changes in the By-laws were approved by the Council and passed by the membership in Executive Session, having been originally proposed by Dr. Richard H. Meade.

Article V, Section 1, of the By-laws should be changed to read as follows:

> The Nominating Committee shall consist of three Active or Senior members who are, by preference, also past Presidents of the Association and in attendance at the meeting. They shall be elected in accordance with the provisions of Article V, Section 1, of the Constitution. The Council shall instruct the Committee as to the vacancies which are to be filled by election.

The following changes in membership status were approved by Council and passed by the membership in Executive Session.

One member was dropped from the rolls of the Association because of nonattendance.

The following Active members were elevated to Senior status:

Arthur H. Aufses
Theodore L. Badger
Edward B. Benedict
Reeve Hawkins Betts
A. Lincoln Brown
W. Emory Burnett
David A. Cooper
Richmond Douglass
Samuel O. Freedlander
Jerome R. Head
Chevalier L. Jackson
Hollis E. Johnson
N. Logan Leven
Oscar S. Proctor
Samuel A. Thompson
Julius Lane Wilson

The following Associate members were elevated to Active membership:

H. William Clatworthy, Jr.
Frederick S. Cross
Preston R. Cutler
George L. Emerson
William W. L. Glenn
Laurence K. Groves
Paul A. Kirschner
Wilford B. Neptune
John M. Snyder
George W. B. Starkey
Rodman E. Taber

The following candidates were elected to Associate membership:

Paul C. Adkins, Washington, D. C.
John B. Blalock, New Orleans, La.
William E. Bloomer, New Haven, Conn.
James W. Brooks, Richmond, Va.
R. Adams Cowley, Baltimore, Md.
Thomas H. Hewlett, Fort Sam Houston, Texas
Lucius D. Hill, III, Seattle, Wash.
Frank E. Johnson, Minneapolis, Minn.
George H. Lawrence, Seattle, Wash.
R. Beverley Lynn, Westbrook, Ontario
James V. Maloney, Los Angeles, Calif.
Dwight C. McGoon, Rochester, Minn.
William T. Mustard, Toronto, Ontario
George L. Nardi, Boston, Mass.
John W. Overstreet, Houston, Texas
David V. Pecora, Ray Brook, N. Y.
Laurence H. Rubenstein, Glencoe, Ill.
Howard D. Sirak, Columbus, Ohio
Joseph J. Timmes, St. Albans, N. Y.
Earle W. Wilkins, Boston, Mass.

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Original Communications

HUGH MORRISTON DAVIES

Born August 10, 1879
An Eightieth Birthday Tribute

Hugh Reid, M.D., F.R.C.S., and G. Penrhyn Jones, M.A., M.D., M.R.C.P., Denbigh, North Wales

THE DOYEN of thoracic surgeons in Britain, Hugh Morriston Davies, was born at Huntingdon, Cambridgeshire, eighty years ago, his father then being in medical practice in the town. This brief communication is intended for a tribute to him as an innovator and pioneer in the field of thoracic surgery and for achieving his professional eminence despite hazards that would have been the despair of lesser men. In the seclusion of the quiet Welsh village of Llanarmon-yn-Ial, he can now survey the years of his labors with serenity and a well-earned content. He is among the last of a privileged generation in British medicine, a select generation, which, recognizing in the early years of this century the inevitability of specialization, pursued its path with that eager devotion characteristic of pioneers.

He received his early education at Winchester College, proceeding to Trinity College, Cambridge, and to University College Hospital, London. In that golden era of medicine he had illustrious teachers, prominent among them Sir Victor Horsley, the neurosurgeon who later died in Mesopotamia in World War I. Morriston Davies's associations with University College Hospital continued following graduation; he became Horsley's surgical assistant and, in 1907, he published a notable paper on the sensory changes in the face following

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Horsley's gasserian ganglion operation for trigeminal neuralgia. For this he was awarded the Cambridge M.D., having already become a Master of Surgery in his old university, as well as a Fellow of the Royal College of Surgeons. He and Wilfred Trotter now began to study the effects of nerve section on themselves, cutting the great auricular, the internal saphenous, and various cutaneous nerves of the arm. Trotter, then a young surgeon on the staff of University College Hospital, later became renowned not only for his surgical prowess but also for his trenchant contributions to philosophical and psychological studies.

At the age of 29, Morriston Davies was appointed to the surgical staff of the University College Hospital, and he then decided to devote particular attention to the diseases of the chest. He managed to obtain a research room in the basement of the medical school and was soon engaged on a study of pulmonary disease, using the new methods and techniques of radiology. In the very next room, Thomas Lewis was pioneering in electrocardiography. It was a period of great technological advance in medicine, and Morriston Davies was in the vanguard of the new clinical science. Hardly anyone in Britain had appreciated the potential value of x-ray in the diagnosis of chest disease; indeed many were sceptical and suspicious of these technical changes in the practice of medicine. Some of his eminent colleagues were even derisive of his tentative excursions into chest radiography. Resolute in his endeavors, however, he did not allow obscurantist opinions to modify his purpose. An incident in 1912 did much to vindicate his sanguine confidence. In that year, a male patient suffering from bronchitis was sent to his department—as a test case for him and his new apparatus. Morriston Davies found a shadow, which he diagnosed as a tumor of the lung. Some of his colleagues would not accept this diagnosis, and it was with consternation that they learnt of Morriston Davies's intention to remove the tumor. Nevertheless the operation was completed—the first dissection lobectomy in the world for carcinoma of the lung. Soon afterward he performed a Wilms' thoracoplasty for tuberculosis and, the following year, the Sauerbruch paravertebral thoracoplasty, both new operations in Britain.

Morriston Davies was already well acquainted with the progress made by the Germans in the now rapidly expanding field of thoracic surgery. At a meeting of the Deutsche Geselschaft für Chirurgie in Berlin in 1910, he had seen the methods used by the German pioneers for rib mobilization, together with the various devices employed by them in open operations on the chest. He then devised his own "Überdruck" apparatus—generally known to his associates as "H.M.D.'s fire-engine." He invented a special tenotome for adhesion section, which he used under radiographic control—there were no thoracoscopes then; he pioneered in Britain the several methods of extrapleural pneumolysis.

This was an inspired and prolific period in Morriston Davies's life, and in those spacious and confident years before the outbreak of World War I, there were ample rewards for men of ambition and endeavor. Now an acknowledged leader in his particular province of surgery, his future success was assured;

he was still in his thirties. One night, however, in the second winter of the war, he experienced a personal disaster that was to change the course of his life, a tragedy that was as dramatic as it was catastrophic.

That night, in January, 1916, he was called to see a patient in the Victoria Park Hospital in London whom he found to be suffering from an empyema; immediate rib resection and drainage were required. As he was closing the chest he was handed a length of catgut which accidentally contained a sliver of glass; the glass pierced the skin of his right hand. The following morning the hand began to swell and became increasingly painful. It was now evident to him that the sepsis he had been treating the previous night had entered and infected his right hand. Suppuration supervened, and the advice of eminent colleagues was sought—physicians and surgeons. Sir Thomas Barlow pronounced his considered opinion; Sir Rickman Godlee urged him to have the arm amputated. Eventually it was left to Wilfred Trotter to incise the hand and forearm. Although the infection now subsided, the damage had been done. The hand was contracted, the fingers were rigidly flexed, distorted, useless.

Morriston Davies then made the hard but inevitable decision that his surgical career was at an end; it was a bitter decision, but it was firmly made. He, thereupon, resigned from University College Hospital, turning from the main stream of surgical practice to the quiet backwaters of the profession of medicine. The humdrum activities of medical boards then occupied his time for a while, but they had little to offer to a man of his adroit ability. As a doctor in a sanatorium on the outskirts of London he found his work to be a little more congenial, but it was still irksome and wanting in stimulus and inspiration to an eager and inquiring mind. He rejected advice to turn radiologist. His only desire was to leave London and find some suitable work in the peace of the countryside.

Just after the War, he learnt that a country sanatorium in North Wales was for sale and, in spite of doubts expressed by his friends, Trotter among them, he resolved to buy the property. This was the Vale of Clwyd Sanatorium near Ruthin, to which he moved in 1918. He had now found a new purpose and direction. The following year his book on thoracic surgery was published, and soon a steady stream of publications, mainly on the surgical management of pulmonary tuberculosis, issued from his pen. About 1921, he embarked again on major surgery, using a new left-handed technique; the fundamental flair was unchanged. Under his direction the Vale of Clwyd Sanatorium became a thoracic center of some import, attracting surgeons to it from all over the world. Morriston Davies was now consultant thoracic surgeon to all the Welsh chest hospitals, and later to similar hospitals in Cheshire and Lancashire. In 1933 he published his standard work on pulmonary tuberculosis; in 1935 he addressed the American Society of Thoracic Surgeons in New York.

By the middle of the 1930's he was an extremely busy man, applying himself to his professional duties with a quite remarkable vigor. His assistants were constantly amazed at the energy he possessed, an energy dedicated to the service of thoracic surgery. He would be ready, to the consternation of some and the admiration of others, to embark on clinical discussion at late hours of the night, after an already hard day of operating and travelling. He seemed to be indefatigable and, in his somewhat elfin appearance, there persists to this day some little intimation of immortality!

He had set his sights high, and he was intolerant of the slipshod and lazy; to the careless he was a hard master. He knew well enough that his own example was the standard, and the success of his endeavors rested on unremitting vigilance. He organized co-operation and teamwork, sometimes by force of will, often by force of character.

At the outbreak of World War II, he concerned himself with special arrangements for military and civilian chest casualties. In 1942 he was responsible in part for the publication, *War Injuries of the Chest.* The Liverpool and North-West Chest Unit flourished under his guidance as chief thoracic surgeon; he was also consultant thoracic surgeon to the Navy and Royal Air Force. In appreciation of his services to the city of Liverpool, the university there honored him with the degree of Master of Surgery. In 1954, the Royal College of Physicians awarded him the Weber-Parkes Prize with the citation "for the prevention and care of tuberculosis."

Morriston Davies is now, by chronological standards, an old man, but his vivacity and robust agility belie it. Logical in thought, wise in counsel, he still contributes readily to surgical debate; but, as he himself puts it, he now operates through the more nimble hands of another generation. He is spare and somewhat stooping in build, with a suggestion of defiance and even of pugnacity about his bearing. Age has wearied neither his resolution nor his ranging curiosity, and that indomitable spirit that once enabled him to triumph splendidly in adversity is fully manifest today. This man walked through a valley of shadows that few experience in this life, but anguish gave him new impetus and tribulation a new purpose. It is for that, and for his manifold contributions to the art and science of thoracic surgery, that we, in admiration, do him honor.

PRESIDENTIAL ADDRESS
CHANGING CONCEPTS IN THORACIC VASCULAR SURGERY

Michael E. De Bakey, M.D., Houston, Texas

MY FIRST thought at this time is to express my sincere and grateful appreciation for the signal honor which you have accorded me as President of this Association. After observing the list of distinguished men who have preceded me on these occasions, my pleasure in receiving this honor is exceeded only by my sense of humility. My next thought is to express my deep gratitude to the other officers of the Association, particularly our Secretary, Dr. Langston, and our executive assistant, Miss Hanvey, who have performed their duties with such diligence and efficiency that mine required little more than occasional concurrence and courteous attention.

In the selection of an appropriate topic for this occasion it seemed to me that, first, it should be sufficiently challenging to merit your attention and, second, it should be related to an area of work in which I have had intensive interest. During the past decade my associates and I have devoted our main efforts and attention to surgical approaches to certain cardiovascular problems. Among these I have been especially concerned with diseases of the aorta and major arteries, and particularly aneurysmal and occlusive lesions. Accordingly, I should like to discuss some of the more significant observations derived from our experience during this period as they pertain particularly to conceptual and technical developments as well as to factors having an important bearing upon successful application of the operative procedure.

In general, the primary objectives of therapy have been removal of the lesion and restoration of vascular continuity. With increasing experience, however, certain modifications in this concept of surgical treatment have evolved, depending largely upon the nature of the disease. In aneurysms, for example, extirpation of the lesion or its complete obliteration is essential. In some instances this may be accomplished by complete excision of the diseased segment, whereas in other instances this purpose may be achieved with greater technical facility by partial excision and endoaneurysmorrhaphy. In occlusive diseases, on the other hand, removal of the lesion is not always essential and indeed in some instances is even undesirable. Under these circumstances the major problem is concerned with the hemodynamic disturbances produced by

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the occlusive process, whether it is of congenital origin, such as in coarctation, or of acquired origin, as in atherosclerosis. Accordingly, the primary objective of therapy in these conditions is correction of the hemodynamic disturbances and restoration of normal circulation. This may be readily achieved by means of the bypass graft without removal of the occlusive lesion, thus

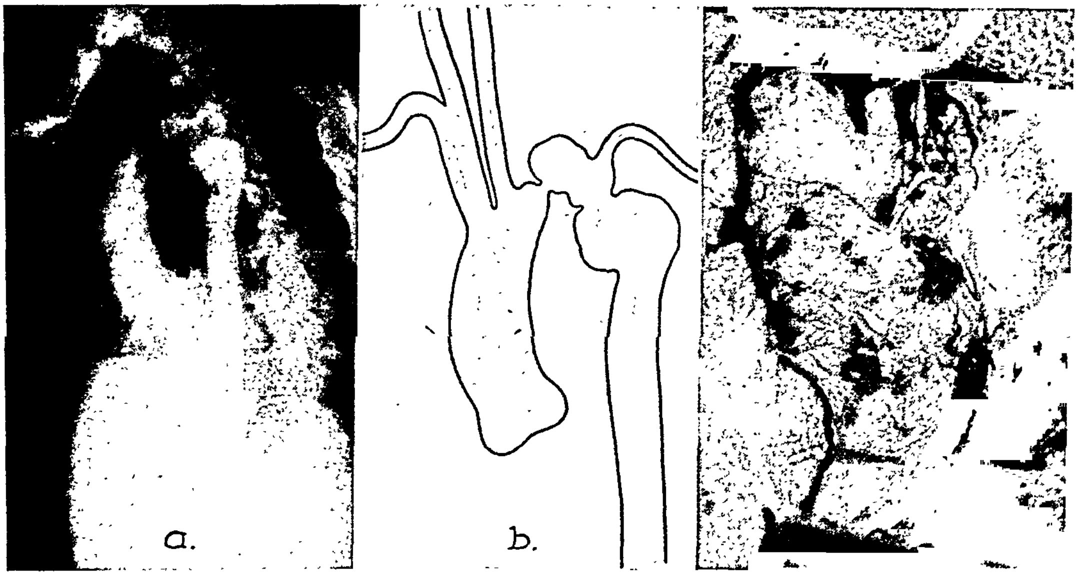


Fig. 1.—*a*, Preoperative angiocardiogram of patient with coarctation of aorta associated with aneurysmal formation, as depicted in *b* drawing. *c*, Photograph made at operation following exposure and immediately before resection of lesion.

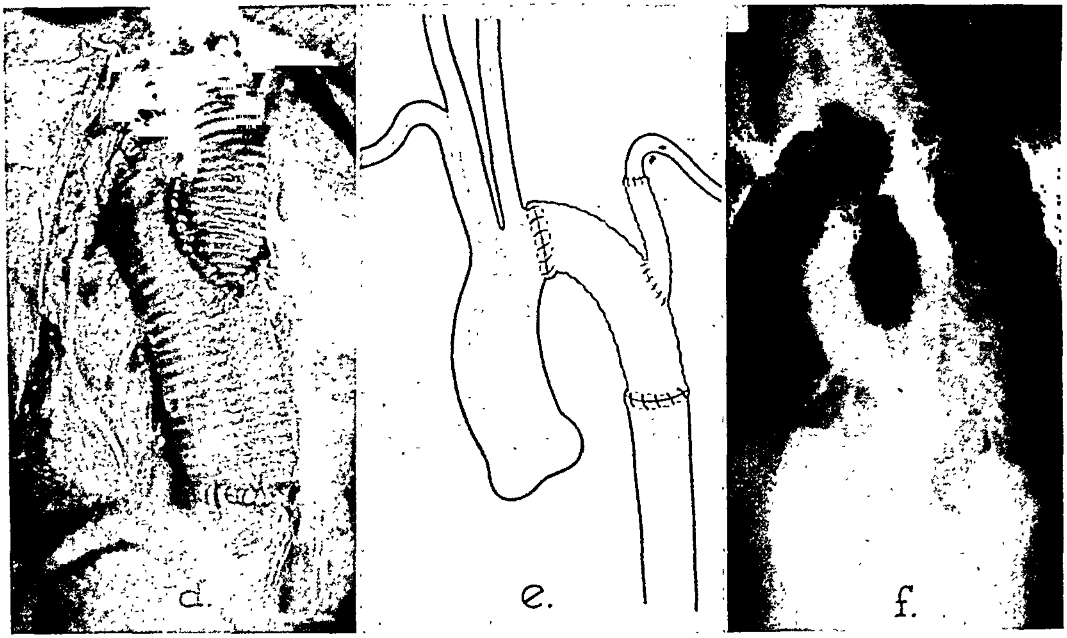


Fig. 1.—Cont'd. *d*, Photograph made at operation showing completed replacement of resected segment of coarctation and aneurysm of aorta with knitted crimped Dacron "graft," as depicted in *e* drawing. *f*, Angiocardiogram in same patient made about 2 months after operation showing normal restoration of vascular continuity and function.

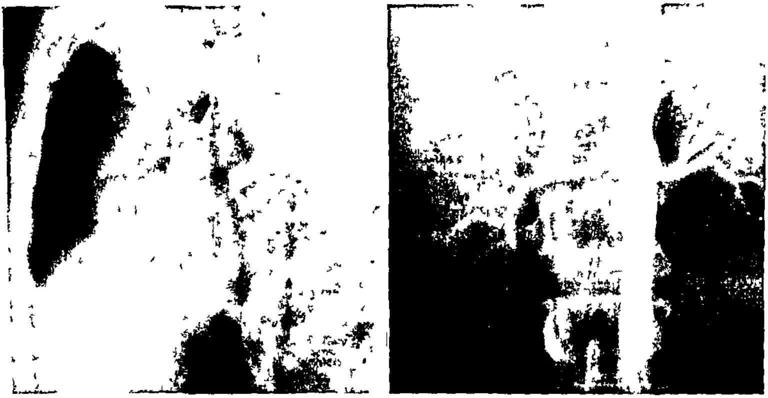


Fig *2A*.—Preoperative angiocardiogram and retrograde aortogram in patient with coarctation involving lower descending thoracic and upper abdominal aorta with marked calcification of latter segment

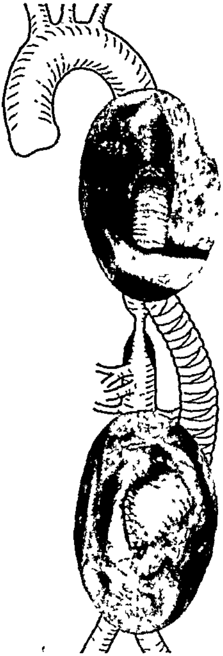


Fig *2B*.—Photographs made at operation with drawings in same patient illustrating application of bypass principle in patient with coarctation of aorta involving lower descending and upper abdominal aorta The knitted crimped Dacron graft has been attached by end-to-side anastomosis to descending thoracic aorta above coarctation and similarly to abdominal aorta below coarctation avoiding some of the difficulties and hazards associated with excision and graft replacement. To be sure, extirpation of the coarcted segment with end-to-end anastomosis or with graft replacement is preferable in most of the usual forms of coarctation and should always be done in those associated with aneurysmal formation (Fig. 1). But in some of the more unusual types, particularly those associated with relatively long coarcted segments extending in some instances into the abdominal aorta, the use of the bypass graft principle has proved to be an entirely effective and much simpler technical procedure (Fig. 2). Similarly, in occlusive lesions involving the major branches of the aortic arch, most of which are of atherosclerotic origin, the bypass graft principle has proved to be the most satisfactory procedure in most cases (Fig. 3). In a small proportion of these cases, in which the occlusive process is well localized and involves only one of these vessels, thromboendarterectomy may be the preferable procedure.

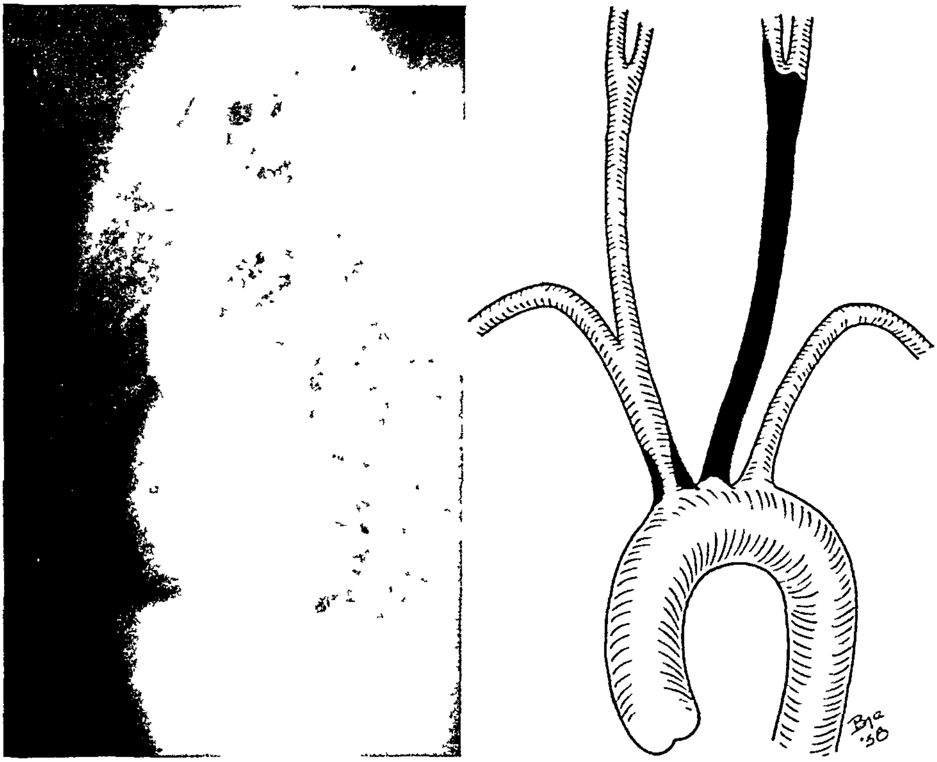


Fig. 3*A*.—Angiocardiogram in patient with atherosclerotic occlusive disease of major branches of aortic arch showing incomplete occlusion of innominate artery and complete occlusion of left common carotid artery, as depicted in drawing at right.

The most important consideration in the application of excisional therapy for aneurysms of the thoracic aorta is concerned with the necessity for temporary arrest of aortic circulation through the segment to be resected. The potentially hazardous consequences of this procedure are increased vascular resistance upon the heart with left ventricular strain and ischemic damage to the tissues distal to the occlusion, most important of which are the central nervous system and the kidneys. In general, this problem assumes increasing significance as the level of occlusion becomes closer to the heart. Control of these factors, therefore, is of vital importance. Several methods may be used for this purpose depending upon the nature, extent, and location of the aneurysm. Among these, hypothermia was first used but, because of certain disadvantages associated with its application, it has been replaced by other methods which have been found superior. For most aortic aneurysms in which the proximal occluding clamp may be applied distal to the left common carotid artery, the most satisfactory method in our experience consists in the use of a pump bypass in which oxygenated blood is removed from the left auricle and pumped into the aorta distal to the occluding clamps through a plastic cannula inserted upward into the left femoral artery (Fig. 4). The major advantages of this method lie in the fact that it provides adequate circulation distal to the level of aortic occlusion to permit viability and even function, as reflected by renal function studies during this period, and to

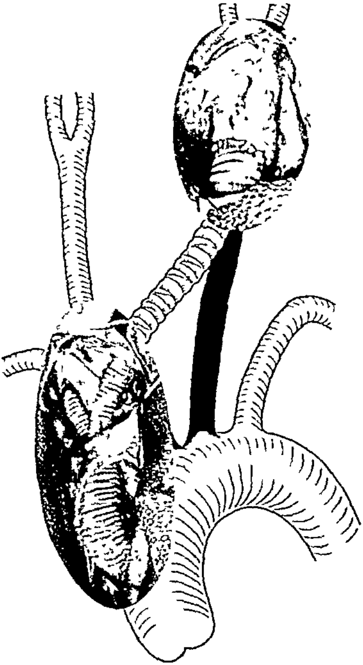


Fig 3B—Photograph in same patient made at operation with drawing illustrating application of bypass principle The bifurcation Dacron "graft" has been attached by end-to-side anastomosis to ascending aorta, and in a similar manner the right limb of the graft has been attached to the right subclavian artery while the left limb of the graft has been anastomosed end-to-end to the endarterectomized distal opening of the left common carotid artery just below the bifurcation

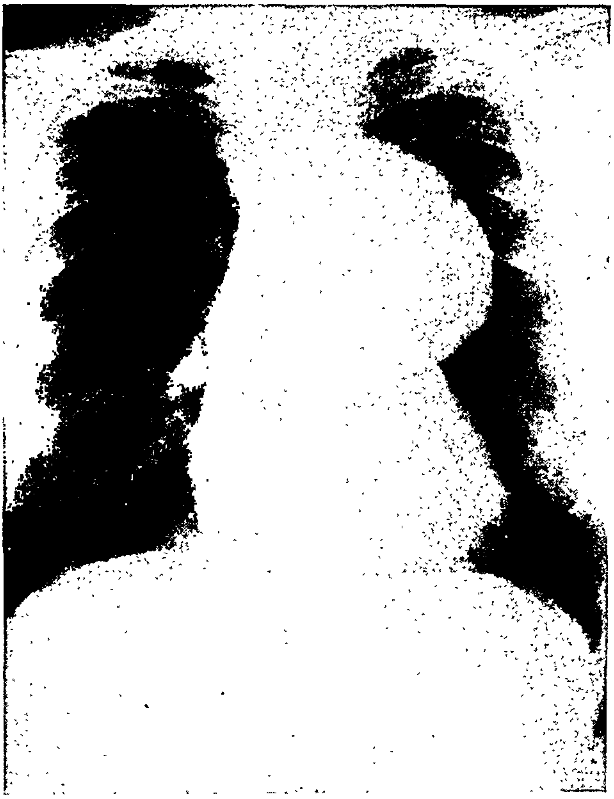


Fig. 4*A*.—Preoperative roentgenogram of chest in patient with large fusiform aneurysm of descending thoracic aorta.

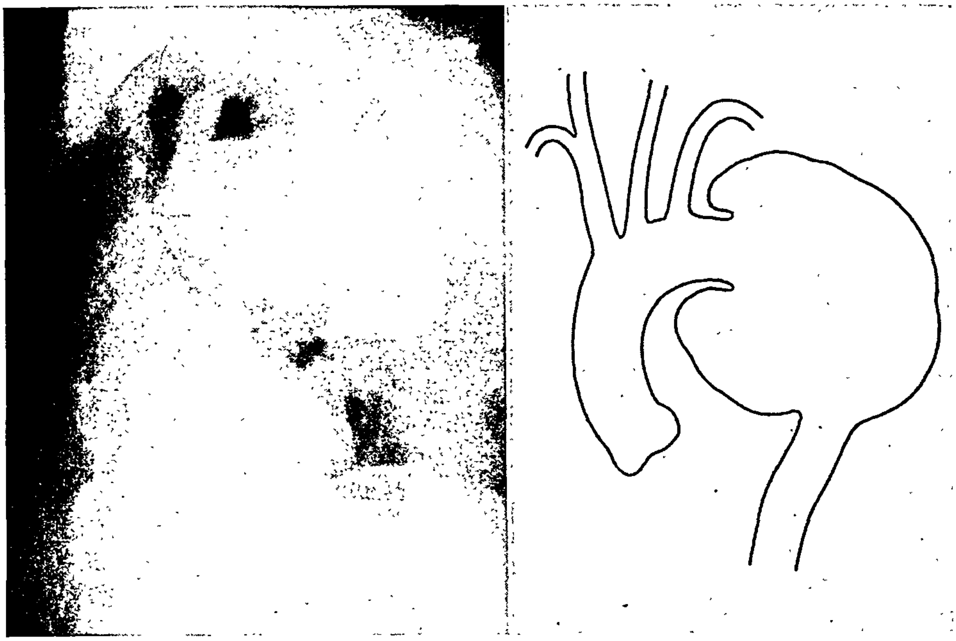


Fig. 4*B*.—Angiocardiogram in same patient showing location and extent of lesion, as depicted in drawing at right.

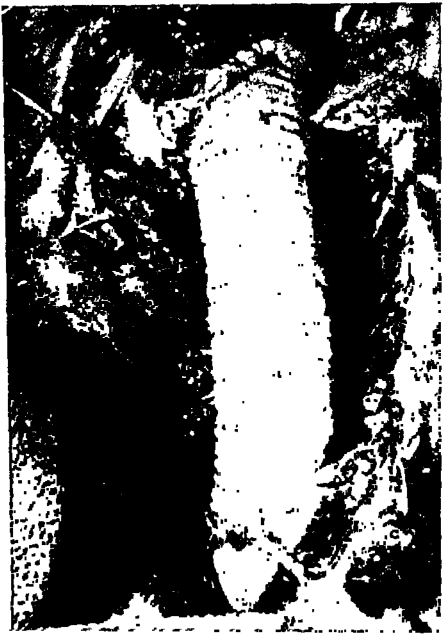


Fig. 4*C*.—Photograph made at operation showing completed replacement of excised segment of aorta and aneurysm with knitted crimped Dacron "graft."

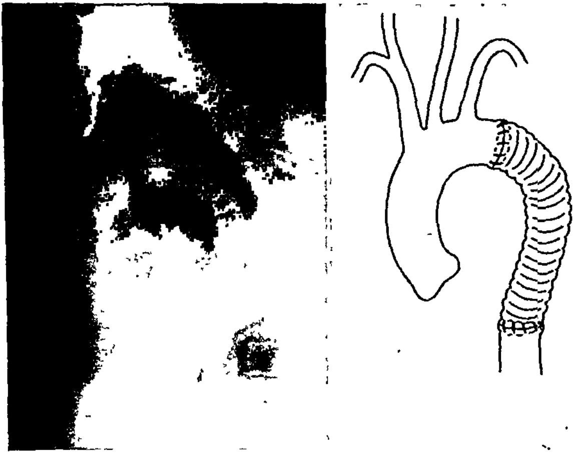


Fig. 4*D*.—Angiocardiogram in same patient made after operation showing relatively normal vascular continuity and function as depicted in drawing at right.

prevent serious left ventricular strain by maintenance of blood pressure at near normal levels. Although this method has been found to be the most satisfactory for aneurysms located in this region, it is not completely effective in preventing spinal cord damage, since among our 55 patients in whom this method was used, some manifestations of this complication occurred in 2. In this connection, it should be noted that in our earlier experience with hypothermia a somewhat similar incidence of the occurrence of this complication was encountered. This remains a rather baffling problem, as it has not been possible to correlate the occurrence of the complication with any significant factors, such as duration of occlusion, extent of resected segment, or pump bypass flow rates. For these reasons, along with other observations, we are inclined to believe that the more significant factors pertaining to this problem include variations in the anatomic pattern and segmental distribution of spinal arteries and development of collateral circulation.

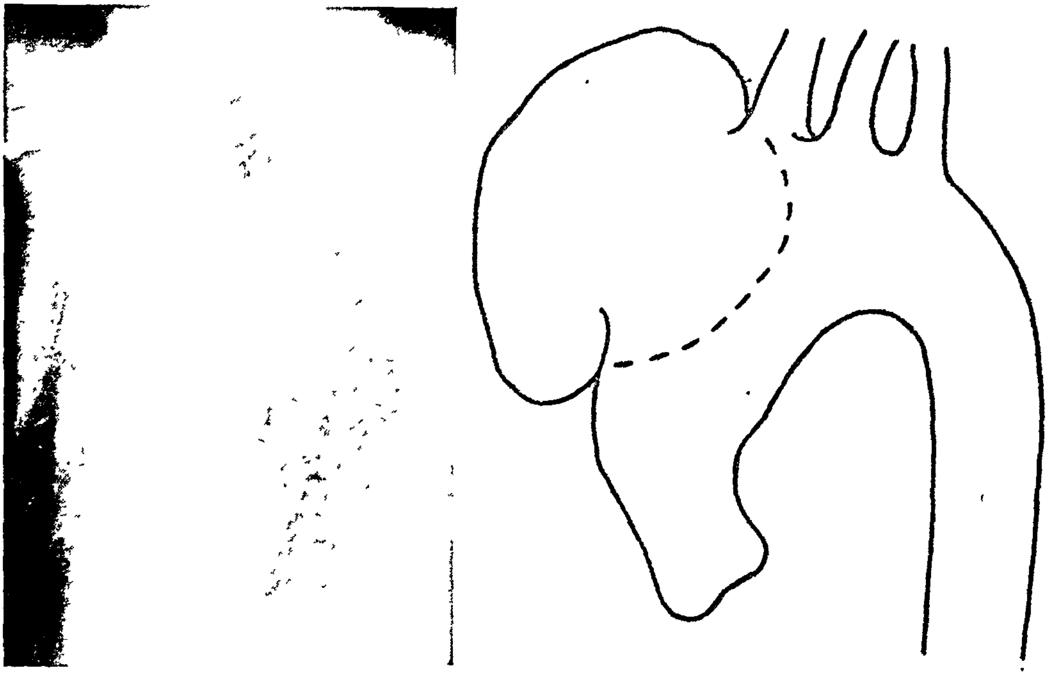


Fig. 5A.—Angioaortogram of patient with large sacciform aneurysm involving ascending aorta as depicted in drawing at right.

Aneurysms involving the aortic arch that are located proximal to the level of the left common carotid artery are associated with much more difficult and hazardous problems, since arrest of aortic circulation at this level, even for a few minutes, may produce fatal heart failure or ischemic damage to the brain. Only in a few cases of sacciform aneurysms with a relatively narrow neck are these problems avoided, since they may be treated by tangential excision and aortorrhaphy. In all fusiform aneurysms, however, and even in sacciform aneurysms with a relatively wide neck that encroaches upon more than half the aortic circumference, measures must be taken to overcome the serious consequences of temporary arrest of aortic circulation at this level. Our experience with several methods which have been used for this purpose

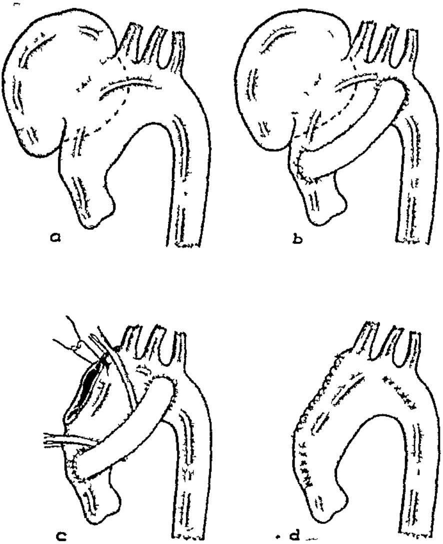


Fig 5B —Drawings illustrating surgical method of treatment employed in this patient utilizing temporary bypass graft to maintain aortic circulation during resection of aneurysm and repair by aortorrhaphy

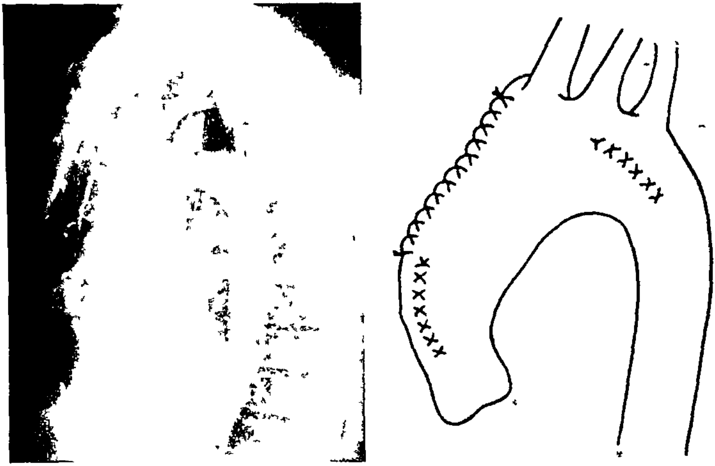


Fig 5C —Postoperative angiocardiogram in same patient showing relatively normal aortic continuity and function as depicted in drawing at right

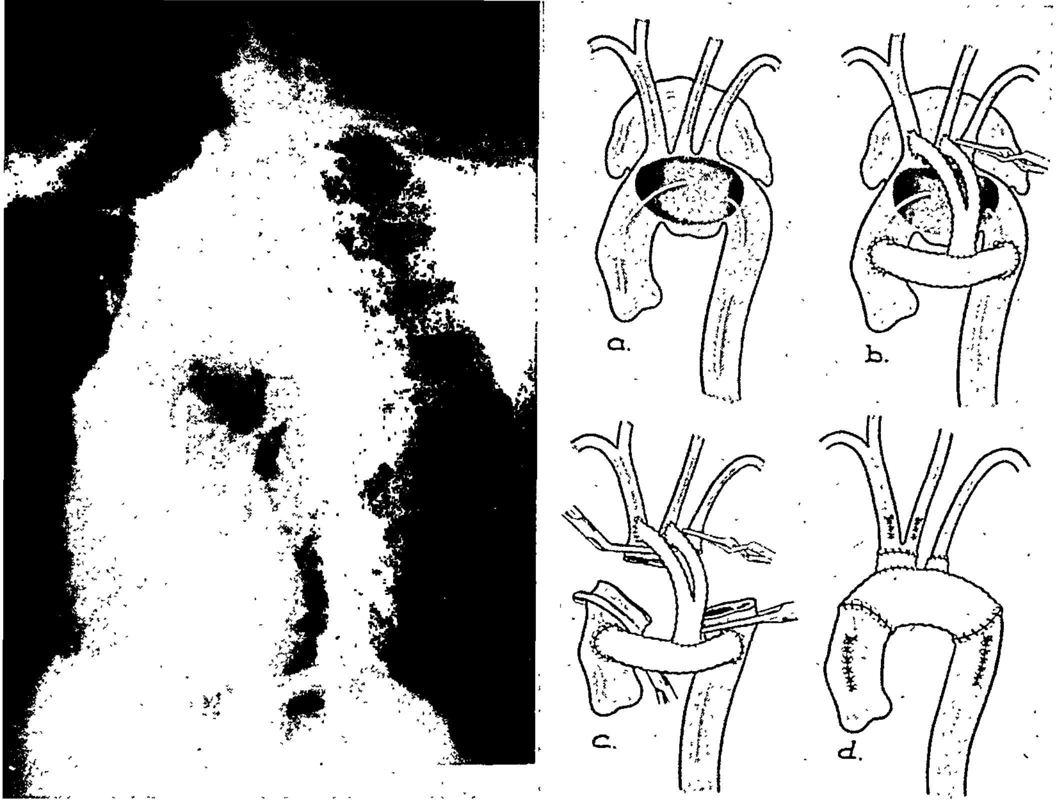
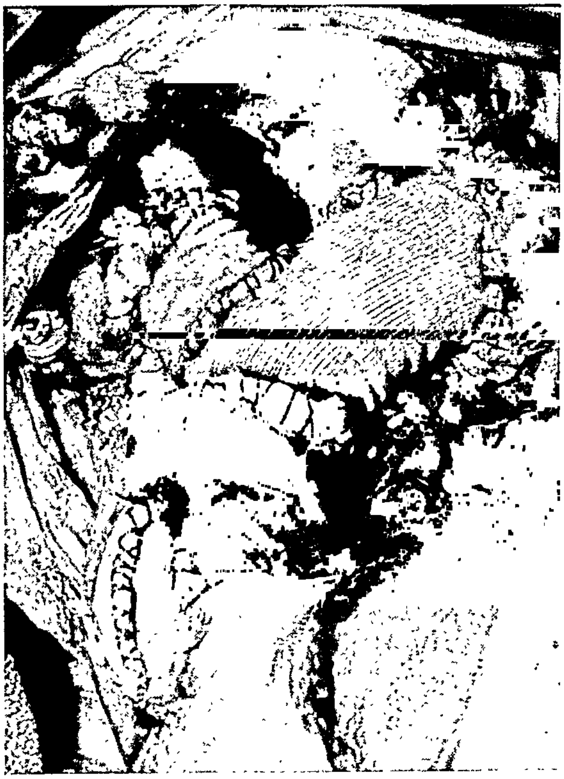


Fig. 6A.

Fig. 6B.



Figs. 6A and 6B.—*For legends see opposite page.*

would suggest that the critical determining factor in their application is the proximal extent of the aneurysm. Accordingly, the major factor in determining the method to be employed is dependent upon whether or not the aneurysm involves the proximal 3 or 4 cm. of the ascending aorta. Thus, in patients without involvement of this segment of the ascending aorta, the temporary bypass principle is employed By this means and with the use of partial

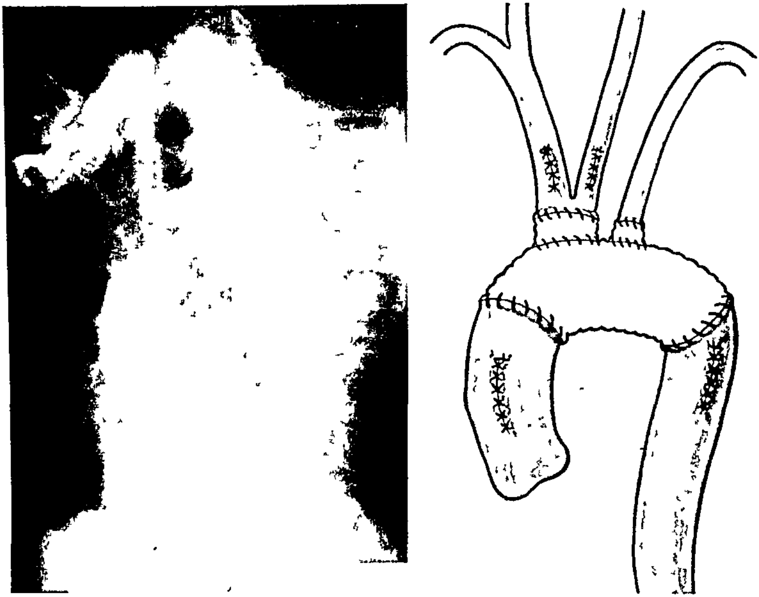


Fig 6C—Postoperative angiocardiogram in same patient showing relatively normal aortic vascular continuity and function in replaced segment of aortic arch as depicted in drawing at right

occlusion clamps and end to-side anastomosis, the bypass graft may be readily applied proximal and distal to the aneurysm after which the aortic segment to be removed may be isolated from the circulation with maintenance of relatively normal aortic circulation during the entire procedure (Fig 5). In patients in whom the innominate and left common carotid arteries are also involved, appropriate branches from the bypass graft are extended to these vessels to provide cerebral circulation (Fig. 6). In this connection two technical principles have been evolved which have enhanced the simplicity and

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Fig 6A—Preoperative angioaortogram showing large fusiform aneurysm involving aortic arch as depicted in drawing (*a*) at right Drawings (*b*, *c*, and *d*) show method of surgical treatment employed in this patient utilizing temporary bypass Dacron graft to maintain aortic and carotid circulation during resection of aneurysm

Fig 6B—Photograph made at operation showing completed replacement of excised segment of aortic arch and aneurysm with Dacron graft including anastomoses to innominate, left common carotid, and left subclavian arteries

facility of the operative procedure. The first is concerned with the application of the bypass graft to the carotid arteries. In some cases, performance of end-to-side anastomosis on these vessels by use of a partial occluding clamp is technically difficult or may be associated with sufficient narrowing of the lumen to interfere significantly with cerebral circulation. These difficulties may be readily overcome with the use of the temporary internal shunt principle (Fig. 7). This can be easily done by use of a No. 14 soft polyethylene tube, approximately 10 cm. in length, which can be inserted through an opening in the artery in the same manner as a T-tube is inserted into the common bile duct, after which the artery is circumferentially tightened against the tube by means of umbilical tapes which had previously been looped around the vessels. While circulation is maintained through this polyethylene tube, the end-to-side anastomosis of the graft to the linear incision in the artery is performed and, just before the last few anastomotic sutures are tightened, the tube is quickly removed and the anastomotic sutures are tightened and tied. By this means cerebral circulation is interrupted for only a matter of seconds.

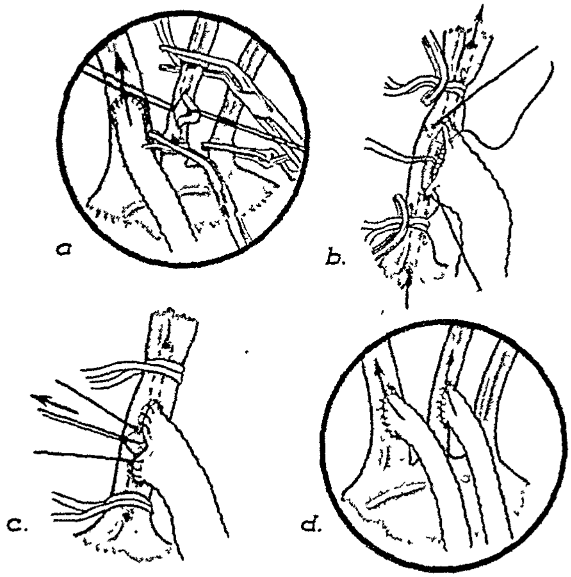

Fig. 7.—Drawings illustrating use of internal shunt principle to maintain circulation in carotid artery during end-to-side anastomosis of graft.

The second principle is concerned with conversion of the temporary bypass graft into the permanent graft. This has become possible with the development of the Dacron tube as a vascular replacement, which may be used as a temporary bypass graft as well as a graft replacement for the excised aortic segment. Although it is not always necessary or desirable to convert the temporary shunt into the permanent graft, under some circumstances it may have a distinct advantage in reducing the extent of the operation, particularly in cases in which the major branches of the aortic arch are involved in the procedure. Its further advantages will be discussed later in consideration of more extensive aneurysms involving both the thoracic and abdominal aorta.

Aneurysms that involve the proximal segment of the ascending aorta constitute by far the most serious and challenging problems in this field of surgery. Under these circumstances it becomes necessary to employ the cardiopulmonary bypass method with use of the artificial heart-lung apparatus. Application of this method imposes certain additional problems some of which have yet to be satisfactorily solved. For one thing, many of these patients are in the sixth to eighth decades of life and are likely to have varying degrees of associated heart disease. Temporary interruption or even decrease in coronary circulation in such patients is poorly tolerated and fatal heart failure may ensue. Second, owing to the necessity for heparinization in application of this method, control of hemorrhage in the grafted segment after completion of the procedure may be extremely difficult, despite the use of measures to counteract heparinization. To be sure, some success has been achieved in application of this method, but an almost equal number of failures has occurred, resulting mainly from the aforementioned problems. It is thus apparent that this represents an area in which there is need for more clinical and experimental investigations, particularly in regard to improved methods of maintaining coronary artery perfusion.

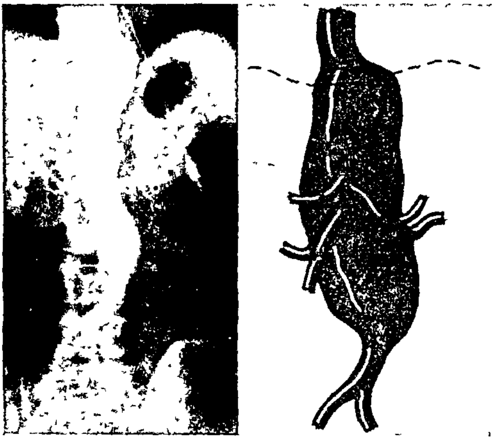

Fig 84.—Preoperative aortogram in patient with large fusiform aneurysm involving lower descending thoracic and upper abdominal aorta including major abdominal visceral branches of aorta as depicted in drawing at right.

Increasing experience in the surgical management of aortic aneurysms and in these various technical procedures has gradually permitted assumption of a more aggressive role in the application of excisional therapy for the more extensive lesions which were formerly considered inoperable. The limitations of this method of therapy have thus been steadily extended. Indeed [illegible] as the lesion itself is concerned, there are now few contraindicat [illegible] section. This is well exemplified by the successful [illegible] of this of treatment in patients having aneurysms involving the entire descending thoracic and upper segment of the abdominal aorta or the lower descending and entire abdominal aorta (Fig. 8). Similarly, patients with separate fusiform aneurysms of the thoracic and abdominal aorta have been successfully treated by this means (Fig. 9). In patients with such extensive aneurysms and particularly those involving the lower descending thoracic and upper segment of the abdominal aorta from which the vital branches of the abdominal viscera arise, the principle of subsequent conversion of the temporary bypass graft into the permanent graft has proved of inestimable value in the successful application of this method of therapy. The extent to which this may be done is illustrated by a case of a huge dissecting aneurysm involving the descending thoracic and upper abdominal aorta which occupied virtually the entire left thoracic cavity (Fig. 10). The knitted Dacron bypass graft was attached by an end-to-side anastomosis to the aorta just distal to the left subclavian artery and then brought down through an opening in the diaphragm and retroperitoneally to be similarly attached to the abdominal aorta just below the renal arteries. With the graft serving as a temporary shunt, occluding clamps were applied to the aorta immediately above and below the aneurysm.

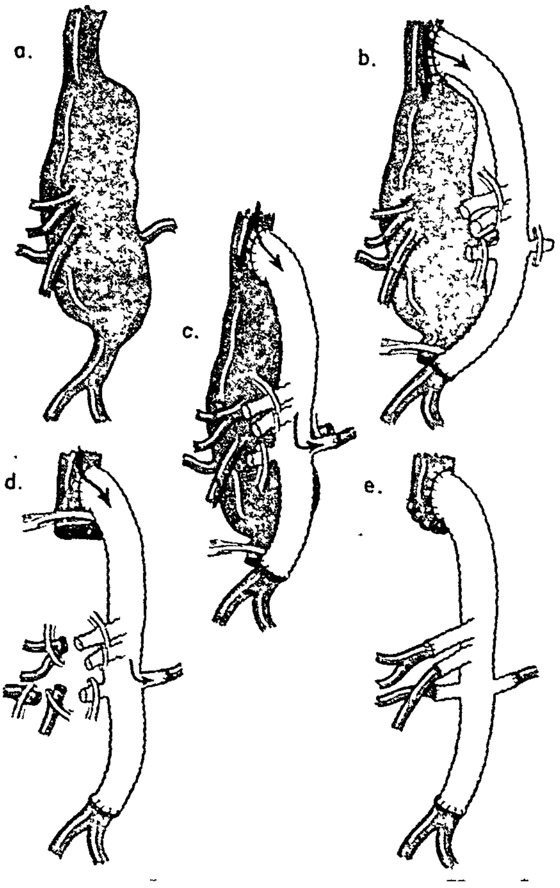

Fig. 8B.—Drawings illustrating method of resection and graft replacement in this patient utilizing principle of conversion of temporary shunt into permanent graft. An important advantage of this method lies in the fact that it minimizes the period of renal ischemia, which is the most critical factor in the operative procedure.

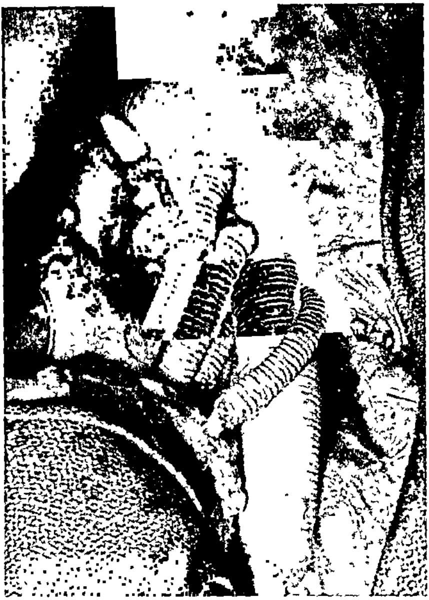

Fig 8C—Photograph made at operation in this patient showing completed replacement of resected segment of aorta with Dacron "graft" including branches to celiac, superior mesenteric, and renal arteries.

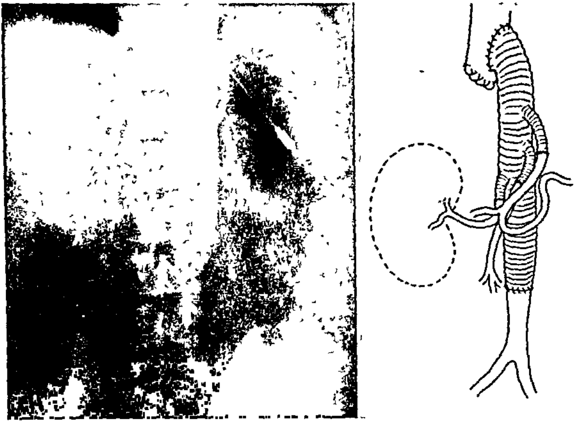

Fig 8D.—Postoperative aortogram in same patient showing restoration of vascular continuity and function through Dacron graft as depicted in drawing at right.

thus isolating it from the circulation and permitting its excision. After completion of this procedure, the openings in the aorta adjacent to the occluding clamps were closed by suture and the occluding clamps were removed. The temporary bypass graft then remained to serve as the permanent graft. Since, during this entire procedure, there was no interference with aortic circulation, no hemodynamic disturbances occurred. Moreover, the extent of operative trauma, duration of anesthesia, and amount of blood lost were greatly minimized. These are factors which, from our experience, have assumed increasing importance in determining the patient's tolerance of the surgical procedure.

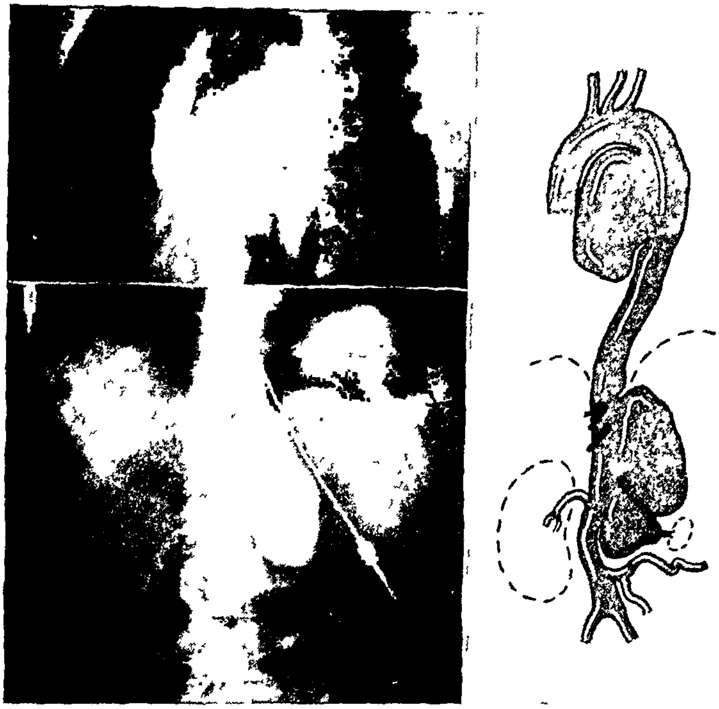

Fig. 9*A*.—Preoperative angiocardiogram and aortogram in patient with large fusiform aneurysm of upper descending thoracic aorta and another even larger fusiform aneurysm involving upper segment of abdominal aorta as depicted in drawing at right. Note that celiac, superior mesenteric, and left renal arteries are completely obliterated with compensatory collateral circulation being provided through enlarged inferior mesenteric artery.

There are, of course, a number of other factors, both systemic and local, which have an important bearing upon the risk of operation. Among the most important of these are advancing age, hypertension, and associated heart disease. The significance of age is well exemplified by the fact that the operative fatality rate for fusiform aneurysms of the descending thoracic

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Fig. 9*B*.—Drawings illustrating methods of aneurysmal resection and graft replacement in this patient. The abdominal aneurysm was resected first, as illustrated by the upper three drawings, utilizing the principle of conversion of the temporary shunt into the permanent Dacron graft. On the fourth day following this operation the thoracic aneurysm ruptured necessitating emergency operation consisting of resection and Dacron graft replacement of the involved segment of descending thoracic aorta by the method shown in the lower left-hand drawing with pump bypass from left auricle to left femoral artery.

Fig. 9*C*.—Angioaortogram made approximately 1 month after operation showing restoration of aortic continuity and function through Dacron grafts in thoracic and abdominal aorta as depicted in drawing at right.

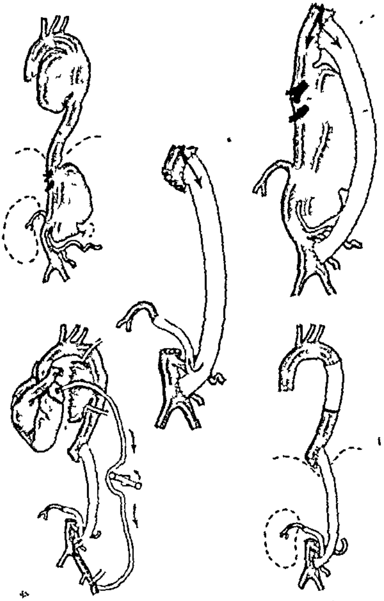

Fig 9B

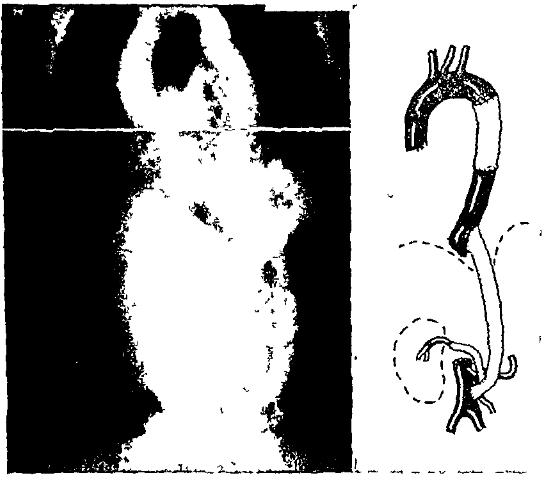

Fig 9C

Figs 9B and 9C—For legends see opposite page aorta was threefold greater in patients in the seventh and eighth decades of life than in those younger than this, the respective figures being 36 and 12 per cent. The importance of hypertension is demonstrated by the fact that the risk in this group of patients was almost three times greater than that in normotensive patients. Probably the most important factor in this regard is the presence of associated heart disease, particularly coronary artery disease, since in our experience the operative mortality in this group of patients was almost five times greater than that in patients without heart disease. There is reason to believe, however, that despite these factors continued improvements in the surgical management of these patients should permit further reduction in the operative risk. This is indicated by the fact that in our most recent series of 62 cases of aneurysms of the descending thoracic aorta in which some of the technical developments just described were employed, the operative mortality was only 15 per cent which is exactly one half of that in our earlier series of 33 cases.

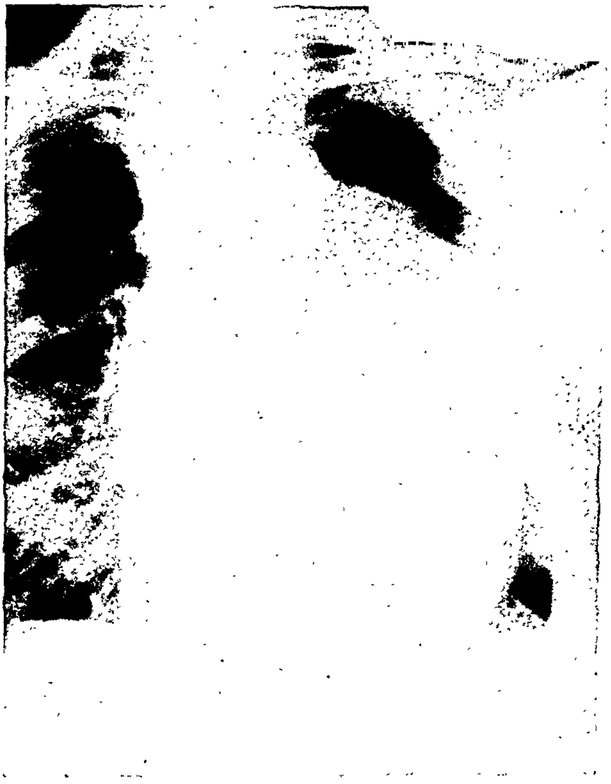

Fig. 10*A*.—Anteroposterior roentgenogram of patient showing large dissecting aneurysm of descending thoracic aorta occupying most of left pleural cavity.

In addition to these tangible factors, which are concerned with the nature of the lesion and with associated local and systemic diseases, there are certain

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Fig. 10*B*.—Aortogram of same patient showing extent of involvement of dissecting aneurysm arising just distal to left subclavian artery as depicted in drawing at right.

Fig. 10*C*.—Drawings illustrating method of surgical treatment employed in this patient utilizing the principle of conversion of temporary shunt into permanent graft as described in text.

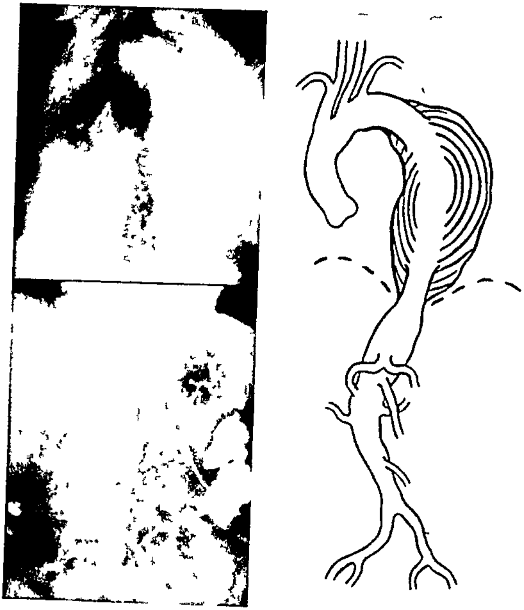

Fig 10*B*

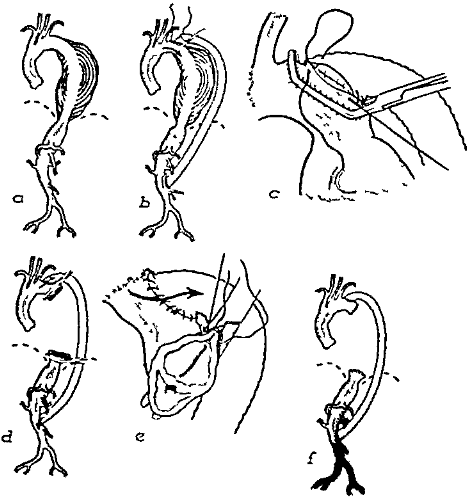

Fig 10*C*

Figs 10*B* and 10*C* —*For legends see*

other considerations, less tangible in character, that also have an important bearing upon the success or failure of these methods of surgical treatment. They pertain particularly to surgical capability, extent of clinical experience, close attention to details, preciseness and dexterity in technical performance, and perhaps the attitude and temperament of the surgeon. To be sure, these are factors of importance in all types of surgery, but there is no field of surgery in which they assume as much significance as in cardiovascular surgery. This is due in large measure to the fact that the margin of safety in this field of surgery is often extremely small. Preciseness in dissection of tissues, in application of a suture, or even in tying a knot may make the difference between life and death. Technical errors which in some other fields of surgery would be considered minor can and do assume vital significance in cardiovascular surgery.

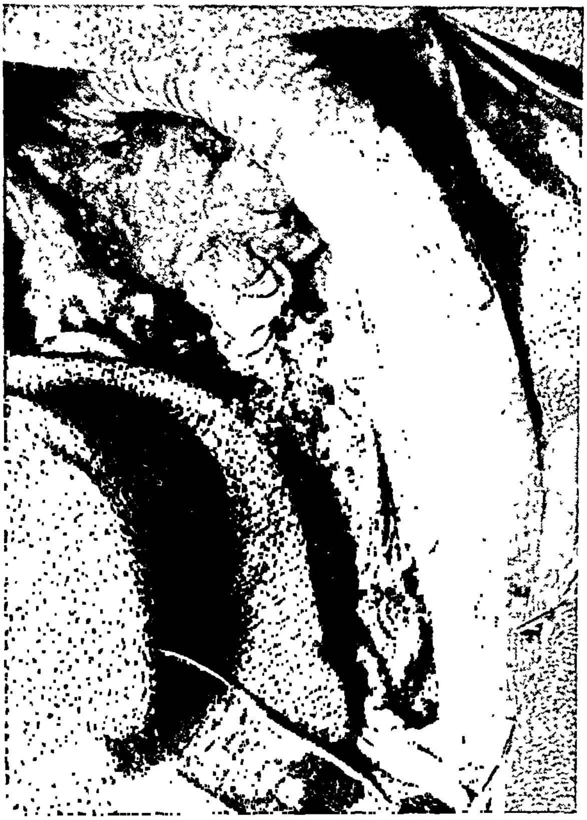

Fig. 10D.—Photograph made at operation following completion of procedure showing functioning thoracic portion of Dacron "graft" with end-to-side anastomosis of graft to descending limb of aortic arch just visible in upper right-hand corner of photograph. Most of abdominal portion of Dacron "graft" lies retroperitoneal.

The relative importance of these intangible factors increases as a result of experience, and cognizance of these matters is of extreme value in the preparation of the surgeon for this field of surgery. The surgeon must be willing to put forth the necessary effort to perfect and refine his technical precision and skill in carrying out difficult procedures if he wishes to attain the highest possible degree of success. Only by arduous attention to these details can he satisfactorily meet the difficult and challenging aspects of these problems. Still another factor, along these same lines that deserves emphasis, lies in the fact that cardiovascular surgery exemplifies so well the importance of fundamental training in general surgery. While one may consider this a highly specialized field of surgery, the need for thorough familiarity with the general field of surgery has been well illustrated by some of the cases to which reference has been made, in which the operative procedure was necessarily extended well beyond the thoracic cavity. Blood vessels have an inherent characteristic of reaching to all parts of the body and do not respect some of the artificial barriers which have been established by specialization. No less important are the various systemic problems of a physiologic or biochemical nature that are often associated with these vascular disturbances. Increasing experience in this field of surgery has led me, like others, to the firm conviction that successful surgical management, as well as progressive developments both conceptually and technically, is best expressed through a broad background in general surgery.

In conclusion, let me say that while the observations which I have presented here have been derived largely from our own experience, I am deeply appreciative of the pioneering efforts and the numerous contributions which have been made by a host of investigators throughout the world. Since many of them are present in the audience, it gives me much pleasure to express these sentiments of high tribute. The truly impressive progress that has taken place in the field of cardiovascular surgery during the past decade provides a brilliant reflection of these efforts. Among the most striking features of these advancements, and undoubtedly important factors underlying their attainment, have been the increasing intensity of research endeavors and the bold ingenuity and aggressive approach characterizing the surgical attack on these grave diseases. As a consequence, many conditions which only a few years ago were considered hopeless are now amenable to effective therapy. No less important has been the fact that these surgical investigations have contributed significantly to greater knowledge and better understanding of the underlying fundamental factors involved in the pathologic, physiologic, and biochemical disturbances of cardiovascular problems. With the continuing vigor and intense activity characterizing the current status of cardiovascular surgery, only the limits of imagination should restrict its progress.

VENA CAVA-PULMONARY ARTERY ANASTOMOSIS

III. Successful Operation in Case of Complete Transposition of Great Vessels With Interatrial Septal Defect and Pulmonary Stenosis

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IN PREVIOUS publications,[1, 2, 3] we reported our experiences gained in animal experiments with vena cava-pulmonary artery anastomosis. In these experiments, the superior caval vein was severed before entering the right atrium, the right pulmonary artery was transsected at its origin with the main pulmonary trunk, and the peripheral stumps of the two vessels were anastomosed by an end-to-end method. In this manner, about half of the systemic venous blood flow bypassed the right heart, and the right lung was supplied with blood directly from the superior vena cava.

Follow-up examinations, after 5 years, of the animals operated upon showed the pulmonary blood flow and oxygen uptake equal on both sides with no increase in venous blood pressure in the area of the superior vena cava. Similarly favorable experimental results were reported by Glenn and associates.[4, 5]

The vena cava-pulmonary anastomosis, as a palliative procedure, has the following advantages over other anastomotic operations: (1) no extra burden is placed on the heart by creating an artificial patent duct (on the contrary, it relieves the overloaded right ventricle of half of its output), (2) by decreasing the blood flow through the right ventricle, it decreases or completely abolishes the right-to-left shunt, (3) the blood pressure in the main trunk of the pulmonary artery is not elevated by this procedure, (4) the anastomosis supplies "pure" venous blood to the lung, providing 100 per cent oxygenation for nearly half of the systemic venous blood flow, (5) endarteritis is less likely to occur, and (6) technically the operation, even on small subjects, is not difficult.

On the basis of our animal experiments, in which the physiology of vena cava-pulmonary anastomosis was studied in detail, it seemed logical that this operation would be beneficial in some types of congenital cyanotic heart

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disease with normal pulmonary vascular resistance, such as tricuspid atresia or stenosis, Ebstein's disease, certain forms of Fallot's tetralogy, among others

CASE REPORT

An 11 year old white boy was admitted to the Department of Thoracic Surgery, Charlotte Memorial Hospital, because of retarded development and shortness of breath On physical examination he was severely cyanotic, and the fingers and toes were clubbed The apical impulse was in the left fifth interspace in the midclavicular line and it was forceful There was a weak systolic thrill palpable over the whole precordium, and a systolic murmur with the same localization The murmur was also audible in the epigastrium, over the aortic arch and carotid arteries The maximum point of auscultation was parasternally in the left second and third interspaces The pulmonary second sound was decreased in intensity

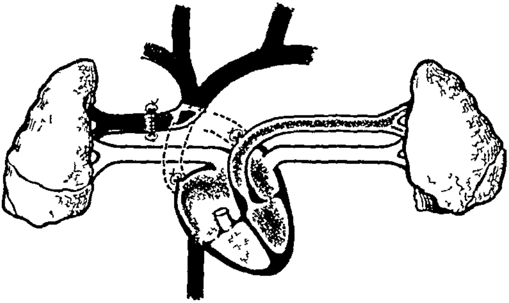

Fig 1—Schema of the operation performed

The red blood cells numbered 5 5 million, hematocrit 54, hemoglobin 15 4 grams per cent, otherwise the routine laboratory data were irrelevant The electrocardiogram showed right sided heart strain On x ray examination, the heart was not enlarged The pulmonary conus was not visible However, the hilar vessels showed moderate enlargement and the peripheral lung fields were avascular The mediastinum was narrow

Right heart catheterization was performed through the prepared right saphenous vein The catheter passed an interatrial septal defect and was later introduced into the right ventricle but not into the pulmonary artery Blood pressure in the right ventricle was 98/3 mm Hg The oxygen content of the blood samples suggested a bidirectional (primarily, right to left) shunt at atrial level and a bidirectional (primarily, left to right) shunt at ventricular level

Following the heart catheterization, an angiocardiography was performed The dye injection studies revealed a large interatrial communication, complete mixing of the blood in the ventricles, simultaneous filling of the retropositioned pulmonary artery, and the right sided aortic arch

With the aim of performing a complete repair of the heart condition, a thoracotomy was performed and an artificial heart lung machine was held ready for cardiopulmonary bypass The exploration revealed complete transposition of the great vessels The small, hypoplastic pulmonary artery arose posteriorly from the left ventricle, and the outflow tract of the right ventricle continued directly in the dilated aorta The condition was considered inoperable and the chest was closed without further attempts of correction

The patient tolerated the procedure relatively well, but 4 to 5 months following surgery his condition showed further, rapid deterioration. The cyanosis increased and he became more and more dyspneic. At this time a second intervention (vena cava-pulmonary anastomosis) was decided upon.

Under endotracheal, ether-oxygen anesthesia, a right, posterolateral thoracotomy was performed in the bed of the resected fourth rib. The superior vena cava and the azygos

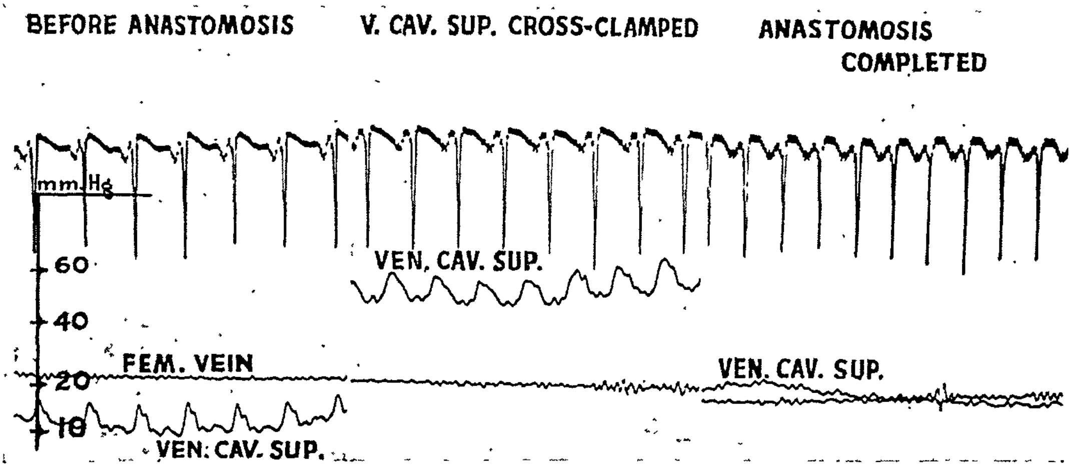

Fig. 2.—Intraoperative pressure tracings of the vena cava superior and femoral vein. (The tracings were taken with a pressure transducer levelled to the operative table, at the time the right pleural cavity was open.)

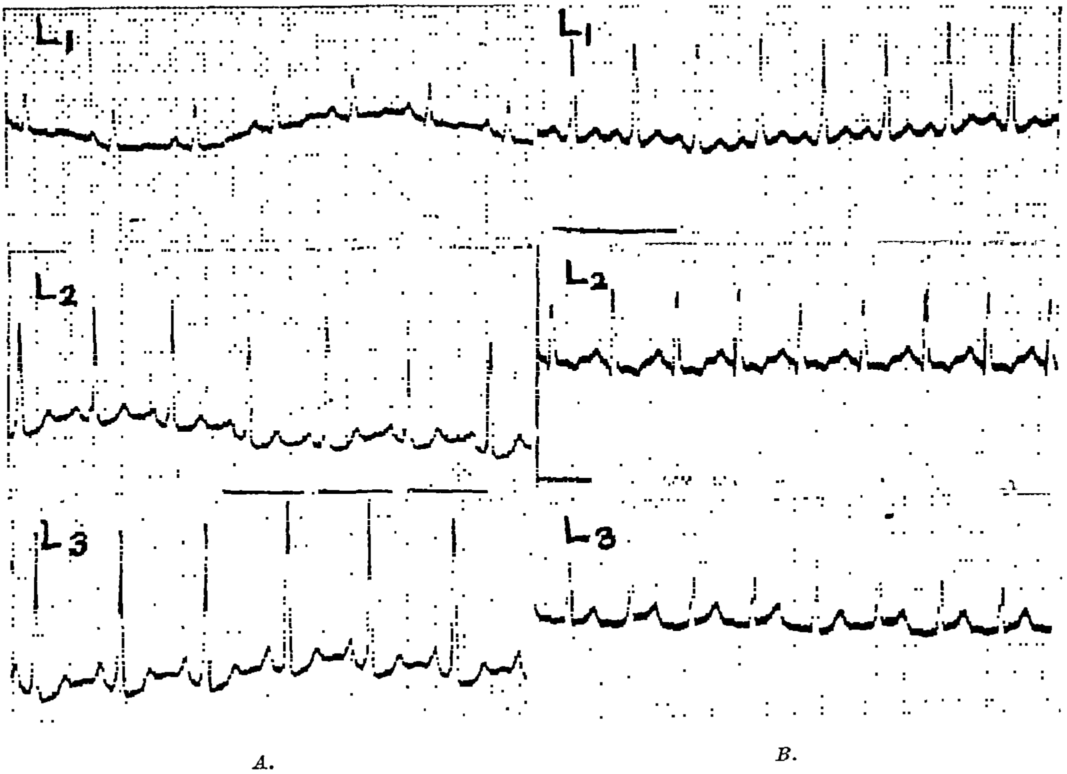

Fig. 3.—Electrocardiogram taken before and 24 hours after surgery. Note the disappearance of right ventricular strain and rotation of the electric axis to the left. *A*, Before surgery. *B*, After surgery.

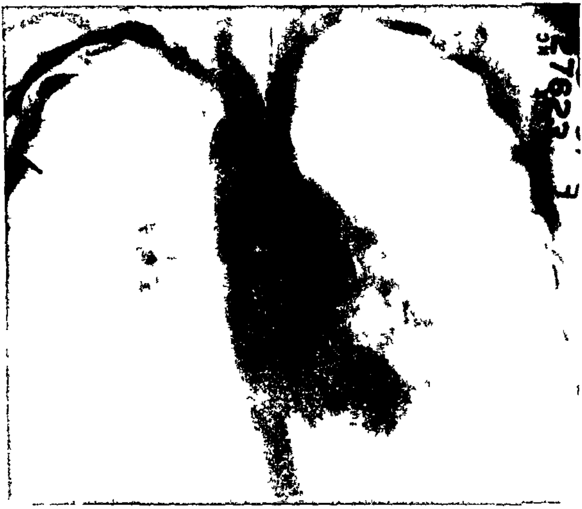

Fig 4—Preoperative angiocardiogram Simultaneous filling of the right sided aortic arch and pulmonary artery Note the avascular lung fields

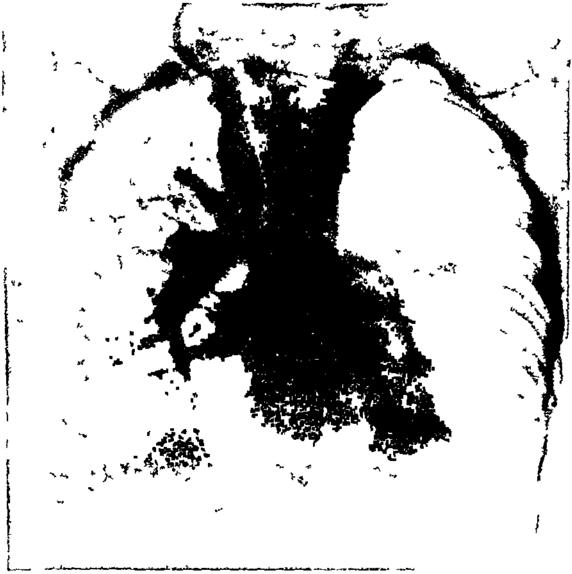

Fig 5—Postoperative angiocardiogram The dye injected into the superior vena cava rapidly fills the vessels of the right lung through the wide vena cava-pulmonary anastomosis

vein were dissected free. The pressures in the systemic venous system were continuously monitored by catheters inserted into the superior and inferior venae cavae. The pulmonary artery was localized rightward and posteriorly to the ascending aorta. The pressure in the pulmonary artery was found to be 16/7 mm. Hg. After freeing the right pulmonary artery, it was ligated at its origin with the main trunk and cross-sectioned distal to the ligature. The peripheral stump was held by a Crawford vascular clamp. Similarly, the superior vena cava was ligated before it entered the right atrium and was severed here. Thereafter, an end-to-end anastomosis was performed between the distal stumps of these two vessels. Upon releasing the clamps, the right pulmonary artery filled well through the anastomosis. The blood pressure in the superior vena cava at the time of the occlusion rose from 17/8 to 58/50 mm. Hg, but fell to 21/19 mm. Hg immediately after completion of the anastomosis. There was no change in the rhythm of the heart, systemic arterial, and inferior vena cava blood pressures. The cyanosis of the face and lips increased significantly during the occlusion of the superior vena cava, but completely disappeared following the anastomotic procedure. An intercostal tube was used to drain the right pleural cavity as the thoracotomy wound was closed in layers.

The patient awakened immediately after the operation and had an uneventful postoperative course. The cyanosis did not return even after moderate physical exercise, which he was able to do without dyspnea. The oxygen saturation of the systemic arterial blood rose from the preoperative 82 to 93 per cent. Angiocardiography, performed on the fourteenth postoperative day, showed rapid filling of the right pulmonary vascular system from the superior vena cava through a wide open anastomosis. An electrocardiogram made after surgery showed the disappearance of the right ventricular strain and the electric axis turned to the left.

The patient was discharged 14 days following surgery and has been followed closely since then. He has good color and no recurrent signs of cyanosis. Venous pressures are essentially normal and he is able to perform normal physical activities without dyspnea.

SUMMARY

After 5 years of animal experiments, the authors performed a vena cava-pulmonary anastomosis on an 11-year-old boy, suffering from complete transposition of the great vessels, interatrial septal defect, and pulmonary stenosis. In the course of the operation, the superior vena cava and right pulmonary artery were ligated proximally and cross-sectioned, and an end-to-end anastomosis was performed between the distal stumps of the vessels. In this way about 50 per cent of the systemic venous blood flow bypassed the right heart and was shunted directly into the right lung. The patient tolerated the procedure well and showed significant postoperative improvement.

The authors recommend the procedure for the treatment of congenital heart disease when pulmonary blood flow is impaired, pulmonary vascular resistance is not elevated, and complete surgical repair cannot be performed because of anatomic reasons or because of the patient's age or general condition (such as, tricuspid atresia and stenosis, hypoplasia of the right ventricle, atresia of the pulmonary artery, and certain forms of tetralogy of Fallot).

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SUPERIOR VENA CAVAL REPLACEMENT

IV. Experimental Use of Alcohol-Preserved Heterografts of Bovine Aorta

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The importance of obtaining a suitable and consistently successful means of superior vena caval replacement and bypass has been discussed in detail in previous communications.[7, 8, 9] Synthetic vascular prostheses and homografts of aorta and vena cava have been shown to be unsuitable.[1, 2] Of the free grafts, only fresh autogenous aorta has been found to be consistently successful with long-term retention of patency and freedom from constriction and thrombus formation.

The present study was carried out to evaluate the suitability of alcohol-preserved heterografts of cow aorta for superior vena caval replacement.

MATERIAL AND METHODS

Healthy mongrel dogs were used. The weight of the dogs ranged from 12 to 30 Kg. A mixture of oxygen and ether, delivered through an endotracheal tube by means of a mechanical respirator, was employed for anesthesia following induction with intravenous Pentothal. A right third intercostal space thoracotomy incision was used. The superior vena cava was dissected free from surrounding structures. Potts coarctation clamps were used to occlude the proximal and distal ends of the superior vena cava and a portion of the superior vena cava was resected. The resected segment of vena cava was replaced with a preserved heterograft of cow aorta. A continuous over-and-over suture of 5-0 arterial silk was used for both anastomoses. The heterografts of bovine aorta were all slightly to significantly larger than the canine vena cava being replaced. The heterograft appeared to function satisfactorily in all animals at the time of placement. The cow aorta has a very thick and firm wall and there was no tendency for the heterograft to collapse. The chest wall was closed in layers and a catheter, which was left in the chest during the closure, was aspirated and withdrawn.

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The segments of cow aorta employed in this study were obtained from a local packing company and were preserved in 70 per cent ethyl alcohol. The duration of storage and preservation in alcohol ranged from 7 to 8 months The heterografts were reconstituted for at least one hour in normal salt solution containing penicillin and streptomycin.

RESULTS

Alcohol-preserved heterografts of bovine aorta were employed as described for the replacement of resected segments of superior vena cava in 11 dogs. Heterograft patency was investigated by cavogram, postmortem examination, or both from 2 days to 18 months following caval replacement (Table I). The heterograft was found to be patent in 9 animals and occluded in 2. The 2 animals in which heterograft occlusion occurred were examined at autopsy 14 and 21 days after operation. The graft was patent in all of 7 dogs in which graft patency was investigated more than 30 days after operation. Two animals are alive 18 months after operation. Recent cavograms have established the patency of the heterografts in both animals (Fig. 1).

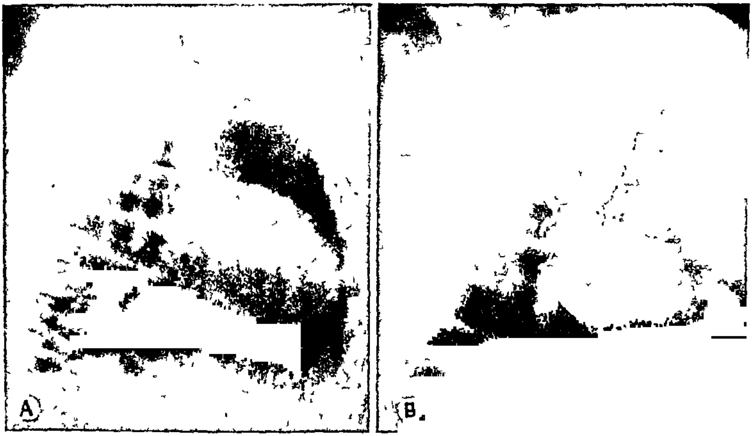

Fig 1.—Cavograms demonstrating patency of heterografts used for superior vena caval replacement (*A*) in Dog 847 and (*B*) in Dog 870, 18 months following operation

The gross appearance of the heterograft was studied at autopsy in 9 animals In 2 of those studied, occlusion of the graft with thrombus formation has occurred. Neither heterograft constriction or thrombus formation was encountered in 4 dogs examined from 2 to 32 days following operation. A few thrombi were found at both suture lines in one animal, 31 days following operation. Nonetheless, this heterograft was patent and showed no e

TABLE I. SUMMARY OF EXPERIENCE WITH ALCOHOL-PRESERVED HETEROGRAFTS OF BOVINE AORTA FOR SUPERIOR VENA CAVAL REPLACEMENT IN DOGS

DOG NO.	WEIGHT (KG.)	PERIOD OF GRAFT PRESERVATION IN ALCOHOL (MONTHS)	INTERVAL, OPERATION TO LAST CAVOGRAM	GRAFT PATENCY AT LAST CAVOGRAM	INTERVAL, OPERATION TO AUTOPSY	GRAFT PATENCY AT AUTOPSY	REMARKS
837	12	8	15 days	Patent	31 days	Patent	Sacrificed; no constriction or thrombus formation
840	24	8			32 days	Patent	Died of pneumonia; no constriction or thrombus formation
841	19	7			31 days	Patent	Sacrificed; no constriction; a few thrombi at both suture lines
846	27	7	4 days	Patent	21 days	Occluded	Died with empyema
847	19	8	18 months	Patent			Alive 18 months following operation; cavograms 4 days, 18 days, 12 months, and 18 months after operation all revealed patency of heterograft
848	17	8	18 days	Patent	12 months	Patent	Sacrificed; graft widely patent without thrombus formation; limited area of contraction in one section of graft
858	30	8	14 days	Occluded	14 days	Occluded	Examined after cavogram; occluding thrombus appeared to have originated at level of distal anastomosis where there was some disparity in size
860	30	8	14 days	Patent	17 days	Patent	Died of pneumonia; no constriction or thrombus formation
869	30	8	5 days	Patent	8 months	Patent	Died of unknown cause; one area of constriction widely patent; no thrombus formation
870	27	8	18 months	Patent			Alive 18 months following operation and in good health; cavograms 12 and 18 months after operation revealed patency of heterograft
873	24	8			2 days	Patent	Died of hemothorax; graft widely patent; no constriction or thrombus formation

of constriction The heterograft in Dog 869 was studied 8 months after placement The graft was patent and free of thrombus formation A degree of constriction was encountered in one area of the graft Similar findings were observed in Dog 848, 12 months after heterograft placement (Fig 2) The constriction which had occurred in one area of this graft had not significantly compromised the lumen of the graft It is of interest that the calcification so often found in long term devitalized, preserved homografts used for arterial replacement was not encountered in either of the 2 animals studied by autopsy, 8 and 12 months following operation

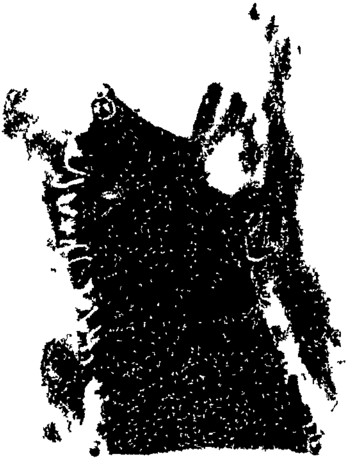

Fig 2 —Autopsy photograph of heterograft from Dog 848 12 months after operation A small area of constriction at one end of the graft may be seen

Microscopic study of the homograft in Dog 848 was carried out 12 months after operation (Fig 3) The graft wall was quite thick The bulk of the graft wall was acellular and essentially amorphous There was no significant invasion of the graft by surrounding connective tissue No microscopic evidence of calcification or thrombus formation was encountered The lumen of the graft had become endothelized

DISCUSSION

Although alcohol preserved heterografts of bovine aorta were not uniformly successful in the replacement of canine superior vena cava, their successful use in 9 of 11 animals is regarded as significant Alcohol preserved heterografts seem to differ from fresh heterografts and those preserved by the freeze drying method Kimoto and his associates[6] have suggested that this

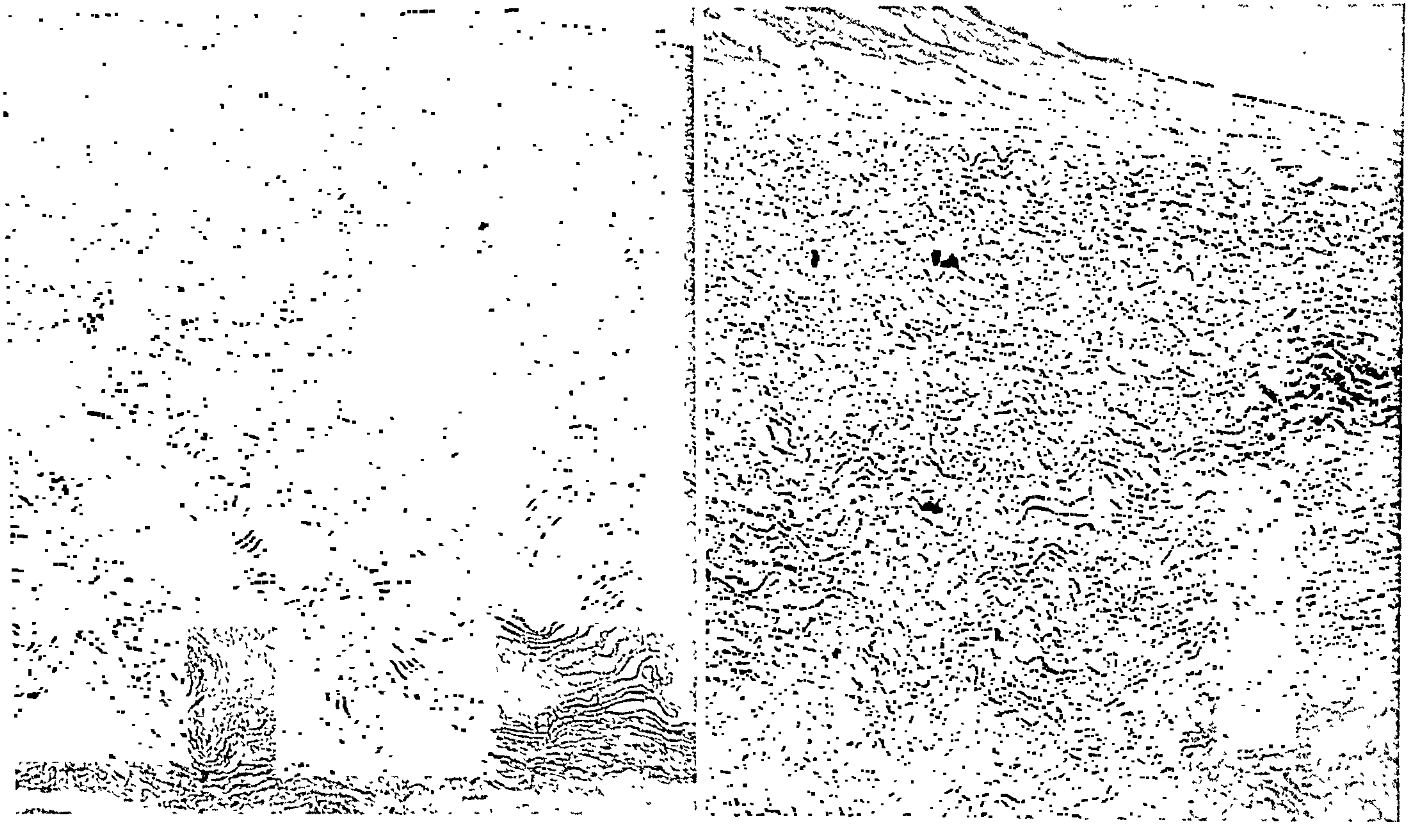

Fig. 3.—Photomicrographs, under low power (*left*) and higher power (*right*), which show thick, acellular, and relatively amorphous, heterograft wall, and absence of significant host connective tissue and vascular invasion in Dog 848, 12 months after operation.

difference might be due to the elimination of some of the untoward antigen-antibody reactions which occur in heterologous transplantation in the viable state. They felt that this alteration might be brought about by the action of alcohol in the dissociation of lipoproteins and the denaturization of other proteins rendering the heterograft serologically inert. They found that heterografts of human arterial segments of viable preservation were successful in replacement of resected segments of the abdominal aorta in only 3 of 8 dogs. When alcohol preservation of the heterografts was employed for periods ranging from 6 to 219 days, the heterograft remained patent in 19 of 21 animals. While rupture occurred in 4 of the 8 heterografts of viable preservation, it was not encountered in the group of 21 animals in which alcohol-preserved heterografts were utilized. The 2 failures in the group in which the alcohol-preserved grafts were used were due to thrombotic occlusion of the heterograft.

The thickness of the walls of the heterografts which rendered them essentially noncollapsible and the greater size of the lumen of the heterograft, than that of the superior vena caval segments they were being utilized to replace, are likely factors in the surprising success experienced with the use of alcohol-preserved heterografts for caval replacement in this study. The use of free grafts larger than the superior vena cava for caval replacement has not been reported. The long-term suitability of thick-walled or rigid free grafts for caval replacement also has not been investigated. Enerson and Galante[3] have reported short-term experiences of 1 to 5 weeks with semi-rigid free grafts of alcohol-preserved homografts which were externally supported by a braided nylon tube. The homograft was secured to the nylon tube with a few interrupted sutures of fine silk. A slightly greater short-term freedom from partial or complete thrombosis was observed in the group of externally supported homografts.

Graft constriction appeared to be a less serious problem with the larger, thick-walled bovine aorta heterografts than with the smaller, more thin-walled homografts. Gerbode[4, 5] found that all of 25 homografts used for superior vena caval replacement had become occluded within 8 months after placement by thrombosis or fibrotic constriction. Some constriction was observed in 2 heterografts, 8 and 12 months after operation. However, the degree of constriction in these larger, thick-walled heterografts did not significantly compromise the size of the graft lumen. It was also of interest that calcification was not encountered in either of these long-term grafts on postmortem study.

The results of this study would appear to justify a more detailed investigation of the suitability for superior vena caval replacement of alcohol-preserved heterografts of relatively large size and thick walls. In addition, the experimental use of some of the newer, more rigid, synthetic vascular prosthetic tubes, in sizes larger than the vena caval segment to be replaced, would seem to be indicated.

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EXPERIMENTAL AND CLINICAL APPLICATION OF A PUMP FOR PARTIAL AND TOTAL AORTIC BYPASS

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A PUMP bypass which shunts blood from the left atrium to the femoral artery provides an excellent system for excision and replacement of the descending thoracic aorta. Our work, reported here, confirms that of De Bakey, Cooley and associates,[1-5] who advocate this technique for managing certain aortic lesions. Our experiments also suggest that the left atrial femoral artery shunt may provide a good solution to the formidable problem of resecting the aortic arch. This type of bypass for the aortic arch has been recommended recently by Johnson[8] and it would have the advantage of being much simpler than the use of a pump oxygenator.[5]

Hypothermia,[6] vascular shunts without pumps,[4] and special anastomotic techniques[9,10] have all been employed to permit resection of the thoracic aorta. These methods have serious disadvantages which the pump bypass largely overcomes. Although hypothermia may protect against spinal cord damage, it does not prevent the hypertension proximal to the site of aortic occlusion which puts a heavy burden on the left ventricle. It could not, of course, be used alone for aortic arch lesions. Vascular shunts from proximal to distal artery without a pump are troublesome, unreliable,[6] and difficult to arrange in the operative field. Special anastomotic techniques are hard to use and have only limited applicability.

A pump system for either partial or total aortic bypass which eliminates many of these difficulties has been studied in dogs and employed clinically for resection of the descending thoracic aorta.

METHODS AND MATERIALS

The pump utilized throughout the experiments was a modified Dale Schuster[3] pump designed by Dr. M. Gliedman, who formerly worked with one of us. The pump (Fig. 1) consists of a flexible Gooch crucible tubing, with a capacity of 80 ml., enclosed in an airtight tube of Lucite. Alternate

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suction and compression is applied on the flexible tubing within the cylinder of Lucite and delivered through a three-way solenoid valve. Originally, a self-regulating mercury switch tripped by the distended tubing was used to regulate the duration of the phases of alternate compression and suction, but this was found to be unreliable. Therefore, it was replaced by a variable electronic timer.* The direction of flow through the pump is regulated by the one-way ball valves. Blood flows into the Gooch tubing by gravity, assisted by external suction in the Lucite tube, and is ejected from the pump by compressed air replacing the suction. The volumetric capacity of the pump and the connecting tubes varied with the speed and duration of filling. It

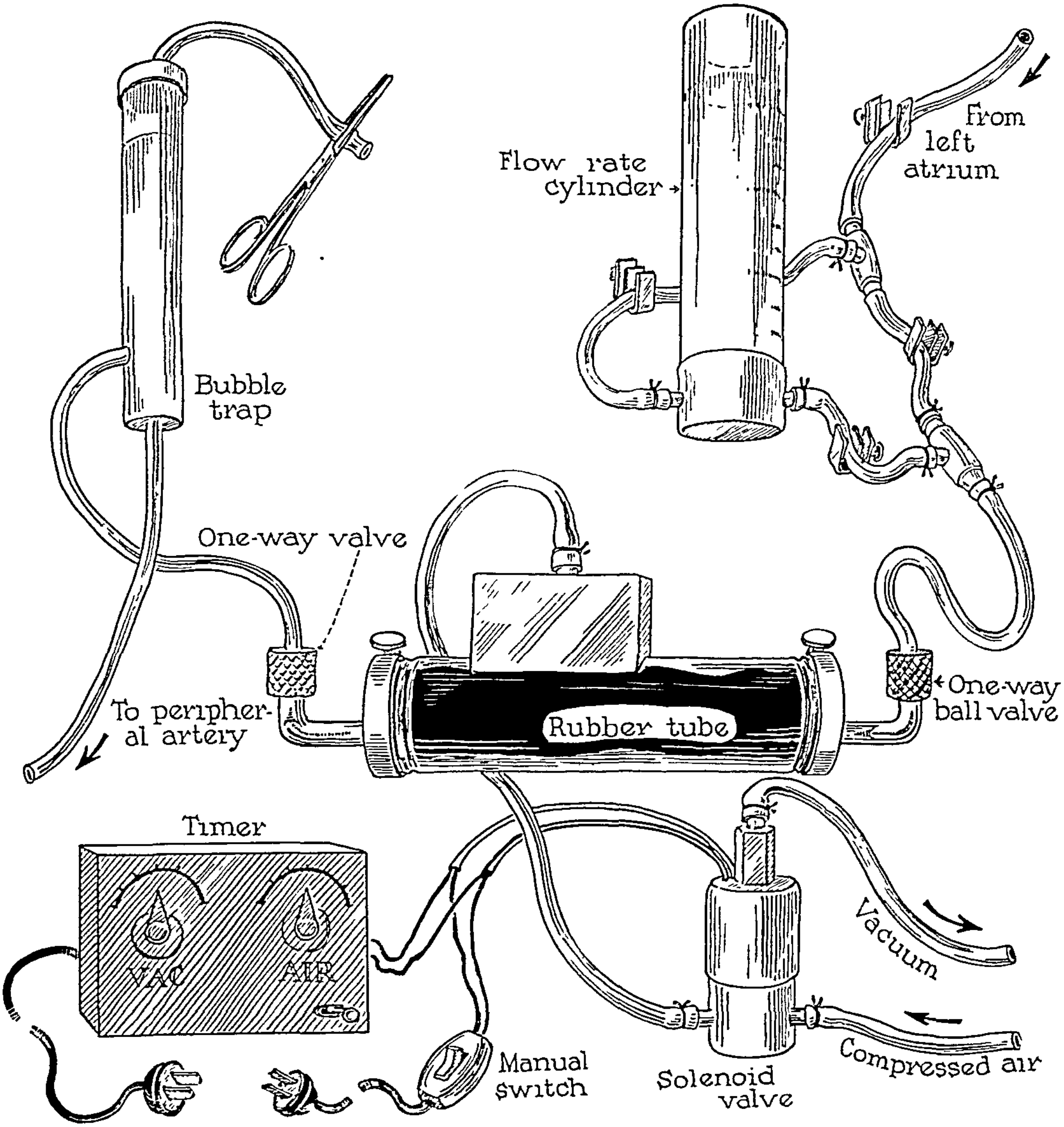

Fig. 1.—The pump used for the extracorporeal bypass.

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*Obtained from G. C. Wilson & Co., Huntington, West Virginia.

varied between 20 and 55 ml. The rate of filling and pumping was adjusted between 14 and 26 times per minute to maintain an optimum flow in the individual experimental animal. For ideal conditions, it was deemed necessary for the filling phase of the pump to be on the average of one and a half times as long as the emptying phase.

Adult mongrel dogs were used throughout the experiments. Anesthesia was obtained with intravenous Nembutal. The femoral and right brachiocephalic arteries were isolated and the left pleural space was entered through the fourth interspace. Heparinization was obtained with 1.2 mg. per kilogram of weight. A No. 18 Fr. flexible plastic catheter was placed into the left atrium and connected to the inflow tubing of the pump and a No. 12 or 14 Fr. plastic Bardic catheter was placed into one of the femoral arteries and connected to the outflow tubing of the pump to complete the bypass. The flexible plastic catheters were found superior to the rather rigid polyethylene catheters of the same size.

In the series of partial aortic bypass, the descending aorta was occluded just below the arch and, for total aortic bypass, the ascending aorta was clamped above the coronary ostia. Distal arterial pressure was recorded by an arterial catheter inserted into the remaining femoral and connected to a mercury manometer. Proximal pressures were recorded by a catheter inserted in the brachiocephalic artery. When the ascending aorta was clamped in the total bypass, the pressure just above the aortic valve or in the left ventricle was recorded through a rigid No. 5 Fr. catheter introduced through the brachiocephalic artery and passed beyond the site of occlusion. Clamping of the aorta was not sufficient to occlude the lumen of this catheter, and reliable pressure readings were obtained.

The duration of the bypass varied from 30 minutes to 90 minutes. After completion of the procedure and removal of the catheters, protamine sulfate was given to neutralize the heparin. Penicillin was instilled into the pleural space before closure and given systemically for one week postoperatively.

Plasma hemoglobin determinations were performed before and at the completion of the experiment as a measurement of the extent of red blood cell destruction. At the time of death or late sacrifice of the experiment animals, histologic studies of the kidneys, liver, and other viscera were obtained.

RESULTS

After standardization of the technique of the bypass with an extracorporeal pump, 26 mongrel dogs comprised the experiment study group. Nineteen of these were subjected to partial aortic bypass and 7 were subjected to total aortic bypass.

Three of the 19 dogs undergoing partial bypass were lost because of technical error during the operative experiment. Only one of the 16 animals surviving the procedure succumbed in the early postoperative period, and this as a result of hemorrhage from the chest wall. The 15 remaining animals were followed from 3 to 60 days and none of these revealed any neurologic disturbances as a result of the cross-clamping of the aorta. At the time of occlusion of the aorta, there was a temporary fall in the arterial pressure distally to between 50 and 70 mm. Hg, but recovery to between 90 and 120 mm. Hg occurred routinely within 2 to 5 minutes. This pressure was maintained for the remainder of the occlusion period (30 to 90 minutes). The arterial pressures proximal to the clamp were elevated 10 to 30 mm. Hg (Fig. 2) above the preocclusion level but appeared to have no adverse effect on left ventricular activity. Plasma hemoglobin levels were generally elevated to a mean value of 142 mg. per cent at the conclusion of the experiments. No correlation between the extent of hemolysis and the duration of the bypass was evident from the data. Platelet counts were not done routinely but, in the animals in which they were carried out postoperatively, they were found to be within normal range. Gross examination and histologic sections of the kidneys and other viscera of dogs, sacrificed from 10 to 64 days postoperatively, were normal, with the exception of the site of occlusion of the aorta. In 2 dogs, narrowing and infiltration with fibrous tissue were seen and, in a third, actual rupture of the intima with a dissecting aneurysm was present. Following a change in the technique of occlusion, this finding was not seen again.

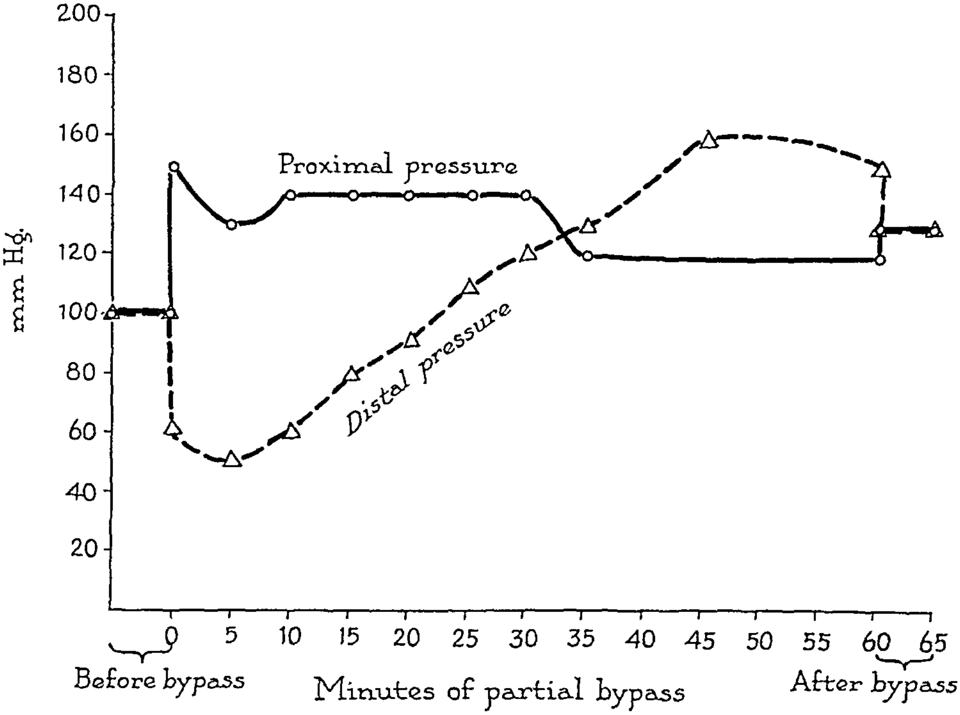


Fig. 2.—Typical blood pressure curve in a partial bypass experiment.

Seven dogs were subjected to total aortic bypass. Two of these died in the early postoperative period. The 5 surviving animals showed no neurologic or other visceral damage. The general pattern of blood pressure levels was similar to those of partial bypass, but the proximal pressures were constantly higher than the distal one by 25 to 50 mm. (Fig. 3). There was no evidence of left ventricular dilatation or failure during the 30 to 90 minutes of aortic occlusion nor upon the release of the occluding clamps at the completion of the bypass.

The successful use of this bypass system with the modified Dale-Schuster pump in the experimental animal to maintain distal arterial circulation, and to prevent excessive proximal arterial pressure levels with possible consequent left ventricle damage, led to its clinical application.

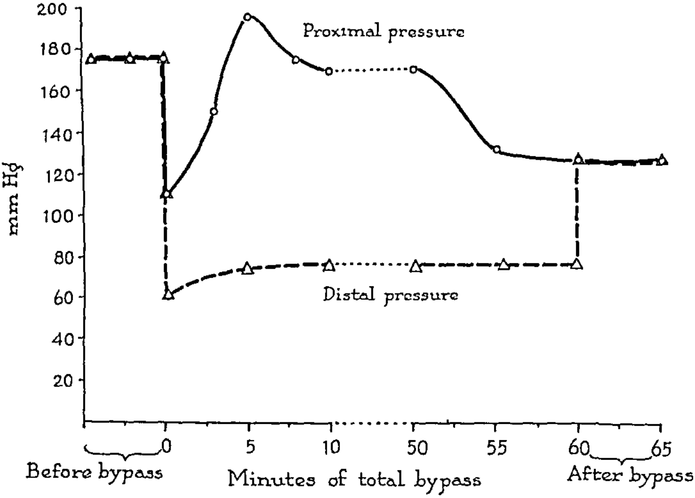
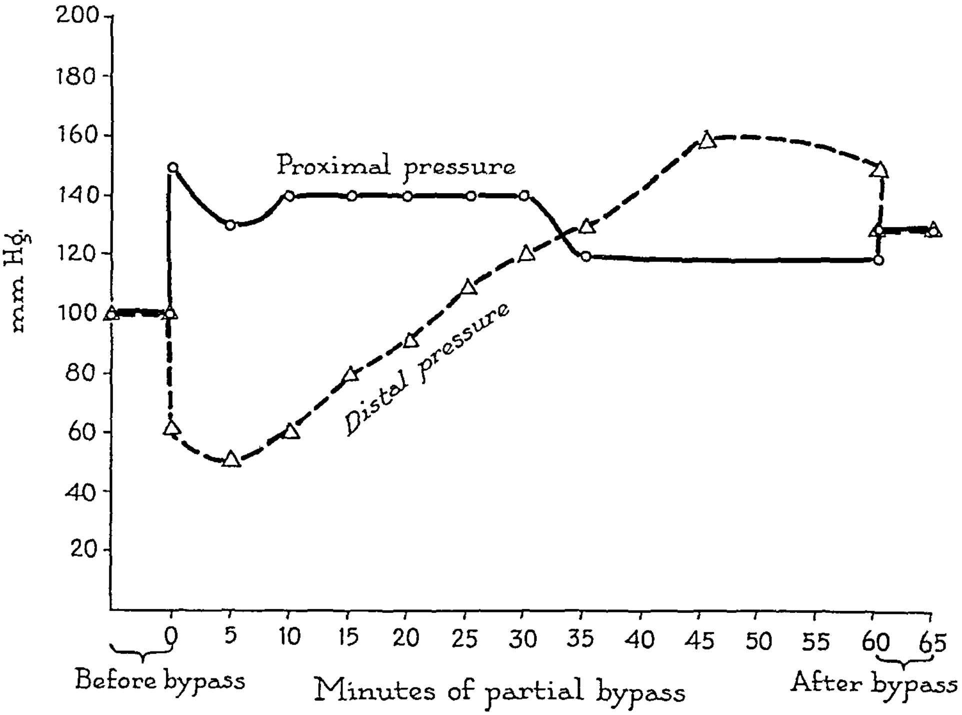


Fig 3.—Typical blood pressure curve in a total bypass experiment.

CLINICAL APPLICATION

A 65-year-old man, with vague complaints caused by an aneurysm of a descending thoracic aorta, was admitted to Veterans Research Hospital in January, 1958, and after a diagnostic investigation he was submitted to operation on Feb. 11, 1958. Under general endotracheal anesthesia, the chest was opened through a left posterior lateral incision, a large aneurysm of the descending thoracic aorta (Fig. 4) was resected and continuity re-established with an Ivalon-nylon aortic prosthesis.[13] The distal circulation was maintained by the extracorporeal pump bypass from the left atrium to the left femoral artery with the pump just described. During the 56 minutes of arterial occlusion and bypass, the distal arterial pressure was maintained between 50 and 60 mm. Hg and the blood flow through the pump averaged 1,100 c.c. per minute. There was no evidence of cardiac dilatation or failure were followed from 3 to 60 days and none of these revealed any neurologic disturbances as a result of the cross-clamping of the aorta. At the time of occlusion of the aorta, there was a temporary fall in the arterial pressure distally to between 50 and 70 mm. Hg, but recovery to between 90 and 120 mm. Hg occurred routinely within 2 to 5 minutes. This pressure was maintained for the remainder of the occlusion period (30 to 90 minutes). The arterial pressures proximal to the clamp were elevated 10 to 30 mm. Hg (Fig. 2) above the preocclusion level but appeared to have no adverse effect on left ventricular activity. Plasma hemoglobin levels were generally elevated to a mean value of 142 mg. per cent at the conclusion of the experiments. No correlation between the extent of hemolysis and the duration of the bypass was evident from the data. Platelet counts were not done routinely but, in the animals in which they were carried out postoperatively, they were found to be within normal range. Gross examination and histologic sections of the kidneys and other viscera of dogs, sacrificed from 10 to 64 days postoperatively, were normal, with the exception of the site of occlusion of the aorta. In 2 dogs, narrowing and infiltration with fibrous tissue were seen and, in a third, actual rupture of the intima with a dissecting aneurysm was present. Following a change in the technique of occlusion, this finding was not seen again.



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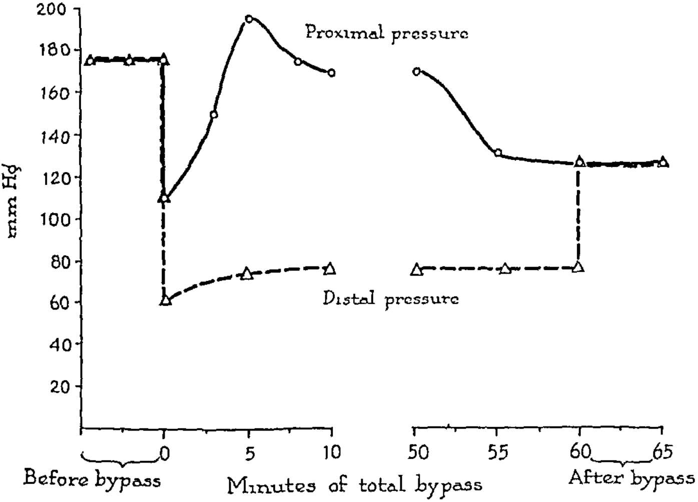

Fig 3 —Typical blood pressure curve in a total bypass experiment.

CLINICAL APPLICATION

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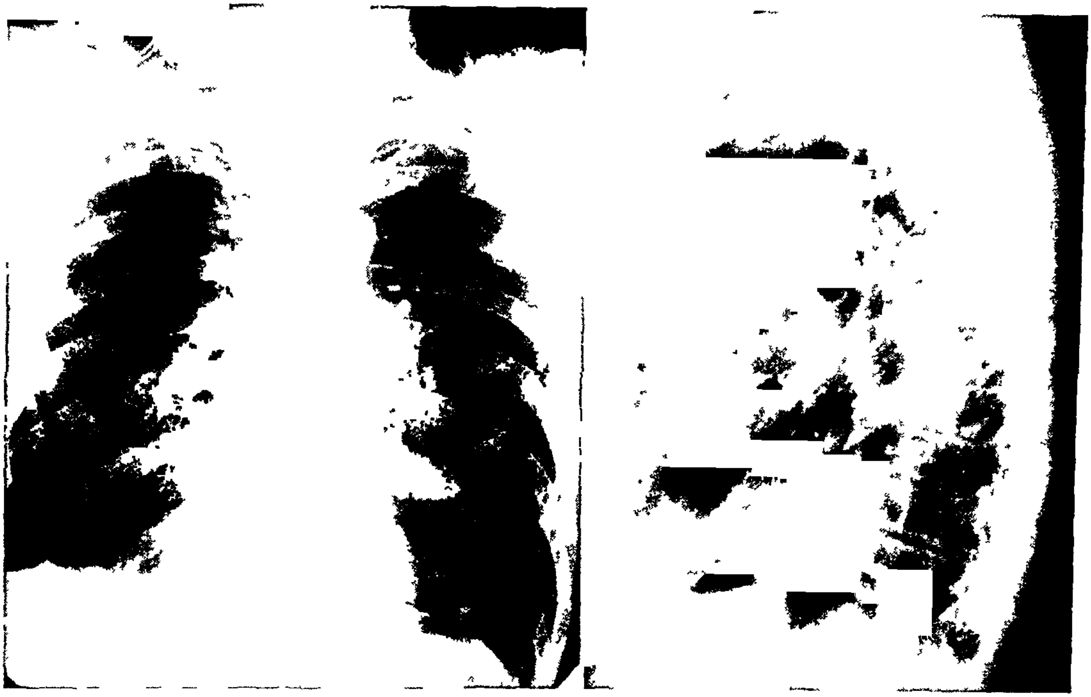

Fig 4.—Preoperative chest x-rays of the thoracic aneurysm which was resected with the aid of the described extracorporeal bypass pump

DISCUSSION

From the experimental data obtained, temporary partial or total bypass of the aorta by means of an extracorporeal shunt from the left atrium to a distal systemic artery with the modified Dale-Schuster pump is a satisfactory method of maintaining the distal circulation. Moreover, proximal hypertension did not develop to any severe degree and no detrimental effects on the left ventricle were noted. The amount of circulation provided distally (flow rates varied with the size of animal) were sufficient to prevent neurologic, renal, or other tissue damage. The method appears to be ideal for bypassing the descending thoracic aorta. The use of this method in treatment of aortic arch lesions is not completely solved. Certainly sufficient circulation around the lesion may be supplied, as demonstrated by the total bypass group, but the technical problems of supplying adequate and continuous circulation to the brain remain.

Mention may be made of intimal damage and dissecting aneurysm resulting from clamping the aorta. These lesions occurred when the aorta was occluded with an umbilical tape and a rubber-tipped glass tube. After changing to a Potts' clamp, no further intimal damage was noted. This result is at variance with the finding of Henson and Rob[7] who found the opposite in a study of the effects of different arterial clamps on the walls of the right gastroepiploic artery in man However, the essential point is that care and gentleness are necessary in clamping a vessel, irrespective of the type of clamp utilized

SUMMARY

A modified Dale Schuster pump is described, and its use as an extracorporeal pump in the partial and total bypass of the aorta is reported Satisfactory distal circulation was maintained from the left atrium to a distal systemic artery with the aorta occluded either proximal or distal to the aortic arch Adverse cardiac manifestations (dilatation or failure) were not noted The usefulness of pump and bypass system is stressed as an aid to surgery of the thoracic aorta

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EXPERIENCE WITH THE BECK FINGER-DILATOR IN MITRAL VALVULOTOMY

Juan José Pérez-Alvarez, M.D., México City, México

SINCE Bailey, in June, 1948, and shortly thereafter Brock and Harken, initiated successfully the surgical treatment of mitral stenosis, utilizing commissurotomes, or performing the "finger fracture valvuloplasty," many surgeons throughout the world have devised a large variety of knives and valvular dilators for the purpose of opening the stenotic mitral valve. This is partially indicative of the different personal preferences of each surgeon, but it also points out the lack of an ideal instrument with which to perform a satisfactory commissurotomy in every case of mitral stenosis.

Ideally, every intracardiac surgical procedure should be done under direct vision. The mitral valve has already been approached in this way in different centers, and open heart correction of its lesions has been performed.[1] But the safety margin of extracorporeal circulation up to the present time, as compared with that of the "closed" technique, is too narrow to be used on patients with pure or predominant mitral stenosis. Consequently, in the centers just mentioned, the open heart technique has been used to correct predominant mitral insufficiency or mitral stenosis concomitant with other congenital or acquired lesions, but not to treat cases of pure mitral stenosis.

Even with a sufficiently safe technique of cardiac bypass, there remains the problem of those patients on whom the valve has been too damaged by the rheumatic process to permit its surgical correction, unless a complete valve replacement with a graft or some kind of prosthesis is accomplished. This, no doubt, will be feasible in the future, but it is also certain that there will continue to be operations for pure or predominant mitral stenosis by the "closed" technique for a time that certainly will not be short.

In 1953, after having tried different commissurotomes, devised by himself or by others, and not finding one completely satisfactory, Dr. Claude S. Beck thought of the device and the maneuver which are the subjects of this paper.

It happened while operating on a patient in whom the stenotic mitral valve had been only partially opened with the finger alone. The orifice, from very small, had been enlarged enough to permit the passage of the index finger up to the first interphalangeal joint, but it would not enlarge any more. At that moment it measured approximately 2 cm. in diameter. The idea of enlarging the circumference of the dilating finger came to Dr. Beck's

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From the Instituto Nacional de Cardiología de México, México City, México.
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mind. For this purpose he wrapped a length of wet cotton tape around the distal phalanx of his finger, and covered this "dilator" with a second glove; re-introducing the finger, so armed, into the auricle, he passed it forcibly through the mitral orifice. Removing the finger from the auricle, Dr. Beck had the second glove and the cotton tape taken off, and then proceeded to explore the valve once more to observe the results The valvular orifice was completely opened, out to the valvular annulus at both commissures, and no regurgitation had been produced (Figs. 1 and 2).

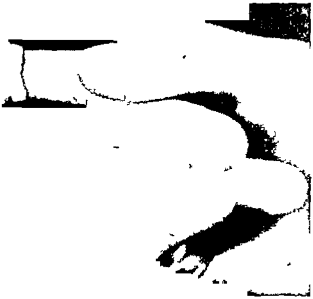

Fig 1

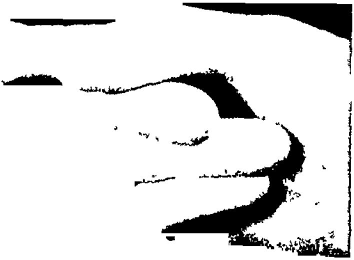

Fig 2

Fig 1 —Cotton tape wrapped around the distal phalanx of the dilating finger to form the dilator

Fig 2 —A second glove is used to cover the dilator.

Since then Dr. Beck has employed the technique described in most of his cases of mitral stenosis and, up to December, 1954, he had operated upon about 200 patients with this procedure[2]

At the Surgical Service of the Instituto Nacional de Cardiología de México, this maneuver has been used since April, 1956 Up to the end of April, 1958, 78 patients with mitral stenosis were operated upon by this technique.

In some of these cases, operative tracings were taken of the left auricular pressure, or of both the left auricular and ventricular pressures simultaneously, before and after performing the valvulotomy, with the purpose of having objective evidence of the effectiveness of the maneuver In these tracings, a substantial reduction of the left auricular pressure, and of the atrioventricular diastolic pressure gradient, can be appreciated (Figs. 3 and 4).

In almost every case in which the procedure has been used, the enlargement of the orifice has extended to the valvular annulus, or very near it at both commissures. This means that the size of the opening obtained has been larger than the size of the dilator. It is easy to understand the mechanism by which this happens: the dilating force, applied eccentrically in all directions, concentrates from the points of greater resistance to those in which the resistance is lesser, in the moment in which the latter start to give in, and is multiplied at these points until the resistance is overcome. In the case of the mitral valve the points of least resistance are the fused commissures.

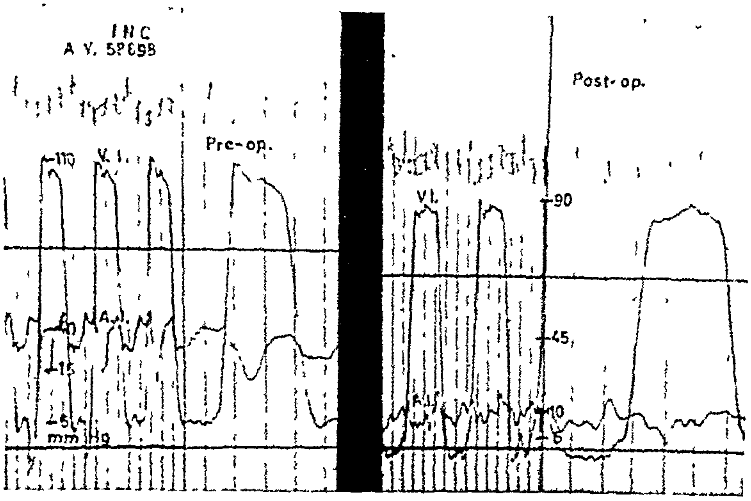

Fig. 3.—Simultaneous electrocardiographic, and left auricular and ventricular pressure tracings, before and after mitral valvulotomy by means of the Beck finger-dilator, in a case of pure mitral stenosis. They show considerable reduction of the left auricular pressure and also of the atrioventricular diastolic pressure gradient. *A.I.*, left auricular pressure tracing; *V.I.*, left ventricular pressure tracing.

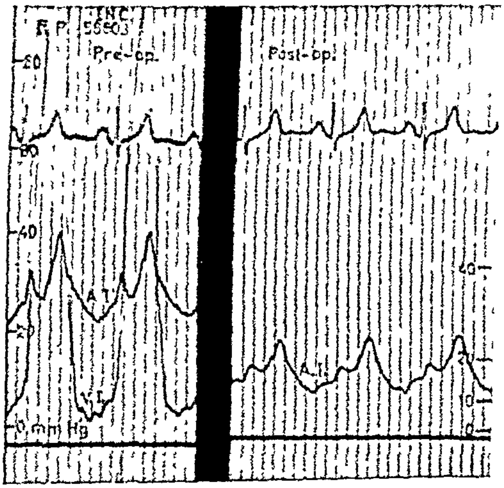

Fig. 4.—The same tracings as Fig. 3 in a patient with predominant mitral stenosis and mitral insufficiency. A left ventricular pressure tracing was not obtained after performing the valvulotomy because the catheter became plugged.

Although the latter statement may be a subject for theoretical discussion, and it might be argued that it is possible that the valve may give in at a point other than the commissures, or become detached from its annulus, the fact is that this has happened neither in Dr Beck's patients, nor in those operated upon at the Instituto de Cardiología It is, of course, necessary to take some precautions in order to avoid the occurrence of such accidents For instance, only a dilator of a reasonable size should be used and, in the event of finding great resistance to its passage through the orifice, a few turns of tape should be taken off in order to make a smaller one Progressively larger dilators may be used in case it is found that the opening has not been sufficiently enlarged at the first attempt

In only 3 of the 78 patients operated upon at the Instituto de Cardiologia was a small regurgitation (that was not present before the valvulotomy) observed by the surgeon after using the technique described, and none was significant In only one case of predominant mitral stenosis with mitral insufficiency, was the already present regurgitation slightly increased In all 4 cases this happened at the commissures or along the valvular orifice just as happens sometimes when the valve is opened with the finger alone or with a commissurotome correctly placed at the commissures That is to say, that the slight regurgitation produced was due to factors such as poor valvular mobility or retraction of the edges of the cusps that impair their correct coaptation In no case was it produced by rupture through the cusps—as may happen when any cutting instrument is improperly used—or by separation of these at their base

The technique has some limitations, one of them is represented by the small size of the neck of the auricular appendage that makes the introduction of the dilator in the auricle difficult This difficulty is actually limited to those cases of marked atrophy of the appendage at its base, and specially those in which there is no visible auricular wall on which to anchor the purse string suture When a small auricular appendage is found, and enough auricular wall is available, the purse string may be extended to the auricle proper, and the same may be done with the incision through which the finger is to be introduced, overcoming the difficulty in this way

Another limitation is produced by the very severe fibrosis of the valve In some cases the healing of the rheumatic process makes the valve tissue become leatherlike, and it resists a reasonable pressure exerted on it with the dilator It is then necessary to start the opening of the valve by means of the instrumental cutting of the commissures, and then to complete its aperture with the finger alone or aided with the dilator This situation was encountered in 4 out of the 78 cases operated on at the Instituto de Cardiologia

Concerning the latter, it must be said that in Dr Beck's experience, as well as in that of the surgical group of the Instituto de Cardiologia, the use of commissurotomes has become exceptional, and the great majority of valves that were resistant to finger dilatation alone have been opened by use of the procedure described

During the period 1953 to 1955 inclusive, 359 mitral valvulotomies were performed at the Instituto de Cardiología de Mexico, 292 of these were performed with the finger alone (81 4 per cent), and 67 were done by using some kind of commissurotome (18 6 per cent) From 1956 to April, 1958, there were 379 mitral valvulotomies of which 280 were done digitally (74 per cent); in 78 cases the Beck finger-dilator was used (20.5 per cent), and in only 25 (6.5 per cent) was it necessary to use some kind of commissurotome.

From what has been written, it may be ascertained that our experience is in accordance with that of Dr. Beck, who has stated: "It is my opinion that this method of opening the mitral valve has almost eliminated the creation of mitral valve regurgitation produced as a complication of valvulotomy. The simplicity of this method, and the almost complete lack of danger of producing regurgitation, enable me to recommend it as the preferable method for mitral valvulotomy. After I began to use this method I found it was not necessary to cut the valve."[2]

There exist two other limitations that are not peculiar to this technique alone, but to every "closed" technique employed to perform a mitral valvulotomy; they are (1) the thrombosis of the auricle, and (2) the calcification of the mitral valve. They represent, at the present time, practically the only causes of death as direct consequence of the operation itself, due to the possibility of embolism to vital organs. Rather than limitations, they should be considered risks that will have to be taken until it is possible to proceed, under direct vision, to the evacuation of the thrombi or the particles of calcium, or even to the total replacement of the valve when it is found too deteriorated to permit its surgical repair.

SUMMARY AND CONCLUSIONS

1. The experience obtained at the Instituto Nacional de Cardiología de México with the use of the Beck finger-dilator in mitral valvulotomy is herein presented.
2. The procedure consists of enlarging the circumference of the dilating finger by means of cotton tape wrapped around the distal phalanx of the finger, and forcibly passing it through the mitral orifice.
3. Of the last 379 mitral valvulotomies, 78 patients who represent 20.5 per cent, have been operated upon under this procedure.
4. The use of commissurotomes was reduced from 18.6 per cent, in which some cutting instrument was used in a previous similar group of 359 patients, to 6.5 per cent in the 379 patients operated upon since the use of the Beck finger-dilator was started.
5. The production of mitral regurgitation, that was not present before the valvulotomy, was minimal, both regarding the number of cases in which it was produced—only 3—and also with respect to its magnitude.
6. The advantages and the limitations of the procedure have been presented, as well as the ways in which the latter may be overcome.

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A PLANNED STUDY OF MINIMAL TUBERCULOSIS

Richmond Douglass, M.D., Edgar M. Medlar, M.D.,† N. Stanley Lincoln, M.D., and E. B. Bosworth, M.P.H., Ithaca, N. Y.

This report presents data from a planned study of minimal tuberculosis regarded as clinically active, treated by bed rest, chemotherapy, and resections of residual lesions; together with detailed pathologic studies of each surgical specimen, and follow-up information.

The approach to the problem of minimal tuberculosis in this way was influenced by several factors.

1. In the fall of 1951 studies at Biggs Memorial Hospital[1] of minimal tuberculosis had shown that, in the pre-drug era, 1 in 5 patients active at diagnosis either had had a relapse of disease or were dead within 10 years.

2. At the start of this study, there had not been time for evaluation of the long-term use of drugs in treating this stage of the disease.

3. The Biggs staff had participated in the original studies of the antituberculous drugs. While their value had been demonstrated, it was recognized that lesions did not resolve completely.

4. The surgical service of this and other hospitals[2] had already shown that operations on lungs involved with tuberculosis were feasible and not unduly hazardous.

5. One of the authors, Edgar M. Medlar, had shown in autopsy studies at Bellevue Hospital[3] that in 96 minimal cases the disease was unilateral in 82 per cent and that in 93 per cent of the reinfection type of disease it was localized in the apical and/or posterior segments. This suggested to us that such lesions should be easily amenable to surgical approach.

6. He called attention to the fact that the group at Sunmount had reported[2] on the excision of 30 localized lesions and had demonstrated the presence of necrotic foci.

7. He had also shown[3] that any minimal lesion of a size which would be visible on the roentgenogram had a necrotic component, which presumably would be the source of an exacerbation if this occurred.

8. Great emphasis had been given to the discovery and treatment of pulmonary tuberculosis in its "minimal" stage, when the disease was considered to be "curable." The programs that had previously been devised toward

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†Dr. Edgar M. Medlar died on June 30, 1956

this goal had lacked one essential element, i.e., a documentation of the exact nature of the pathologic process present in minimal cases. One of the purposes of the present study was *to document in detail* the pathologic features found in the tissues resected during treatment with chemotherapeutic agents. From a study of this nature, it seemed probable that *the dynamics of the* pathologic process could be determined.

The staff decided to study the concept that *minimal tuberculosis* be considered a surgical problem on the basis that resection of residual necrotic lesions would prevent relapses of the disease. It was the aim to include all patients classed as minimal active (and which had never been known to have more extensive disease), to treat them with antituberculous drugs in the then currently accepted manner and to excise the residual lesions.

Diagnosis was based on a positive tuberculin and an unstable lesion as seen in serial x-rays. Demonstration of tubercle bacilli was not required. All patients diagnosed as having minimal active tuberculosis were included, the exceptions being a few who declined surgery. Complete roentgenographic studies, including planigrams in all but a few, were carried out. All recognizable foci, including bilateral lesions, were considered indications for proposing surgery. At operation the collapsed lung was carefully palpated and the location of all lesions noted. An effort was then made to excise all areas of disease utilizing such surgical approach as was best suited.

The group studied consisted of 104 patients of whom 15 had bilateral excision. The operations were done between September, 1951, and December, 1955, inclusive. There were 43 males and 61 females, with 24 under 20 years of age, 68 between 20 and 39 years of age, and 12, 40 years of age or over (Table I).

TABLE I. RESECTION FOR MINIMAL TUBERCULOSIS PATIENTS BY AGE AND SEX

SEX	AGE (YEARS) 10-19	20-29	30-39	40-49	50-59	TOTALS
M	10	14	11	5	3	43
F	14	25	18	3	1	61
Totals	24	39	29	8	4	104
			Bilateral Patients (included in above)			
M	2	-	1	-	-	3
F	1	4	6	1	-	12

The type of chemotherapy varied as the usage of drugs changed, and new drugs became available. Sixty patients received streptomycin, and para-aminosalicylic acid (PAS), while 43 received *isoniazid in some combination.* One patient received no drug therapy. The drugs were used until it was felt that maximum clearing had occurred. The preoperative duration of such therapy was 4 months or less in 36; 5 to 8 months in 56; and over 8 months in 11 (Table II). Concentrate negative sputum was the rule at operation, but was not required.

TABLE II RESECTION FOR MINIMAL TUBERCULOSIS
PREOPERATIVE CHEMOTHERAPY—104 PATIENTS

DRUGS	PATIENTS	MONTHS OF CHEMOTHERAPY (PREOP.) 0-4	5-8	8 OR OVER
SM* + PAS†	60	21	30	9
SM + INH‡	22	10	12	–
PAS + INH	14	4	9	1
SM + INH + PAS	6	–	5	1
INH + PZA§	1	1	–	–
Totals	103	36	56	11
No drug given	1			

*Streptomycin †para aminosalicylic acid ‡isonicotinic acid hydrazide §pyrazinamide

Postoperatively, drugs were at first given to cover the recovery period only, but when excised specimens showed areas of new disease to have occurred during drug therapy, the drugs were arbitrarily given postoperatively for 4 months. During this period, a graduated program of increasing activity was carried out with discharge at the end of 4 months. Twenty-eight patients had received postoperative drug therapy for 2 months or less, 16 for 3 months, 56 for 4 months, and 3 more than 4 months following surgery (Table III).

TABLE III RESECTION FOR MINIMAL TUBERCULOSIS
POSTOPERATIVE CHEMOTHERAPY—104 PATIENTS

DRUGS	PATIENTS	MONTHS OF CHEMOTHERAPY (POSTOP.) 0-2	3	4	OVER 4
SM + PAS	60	24	9	26	1
SM + INH	19	1	6	12	–
PAS + INH	19	1	1	15	2
SM + PAS + INH	4	2		2	
PZA + INH	1			1	–
Totals	103	28	16	56	3
No drug given	1				

The bacteriologic studies showed 25 with positive smears of concentrated sputum, 50 with positive cultures of sputum or gastric contents, and 29 negative on initial study. Prior to operation 18 of the 25 had converted on smears of concentrates while 48 of those positive on culture had converted to negative (Table IV).

TABLE IV RESECTION FOR MINIMAL TUBERCULOSIS
SPUTUM STATUS

SPUTUM BEFORE CHEMOTHERAPY	SPUTUM BEFORE OPERATION CONC +	CULT +	CULT −	TOTALS
Conc +	7	2	16	25
Culture +	2	–	48	50
Culture −	–	–	29	29
Totals	9	2	93	104

The major complications of surgery included 5 hemothoraces, one of which was massive, 3 bronchial fistulas and 3 others (Table V). The incidence of complications decreased as experience was gained, all responded to therapy

TABLE V. RESECTION FOR MINIMAL TUBERCULOSIS
MAJOR POSTOPERATIVE COMPLICATIONS
119 OPERATIONS—11 COMPLICATIONS—9 PATIENTS

Massive hemothorax	1
Limited hemothorax	4*
Empyema	1*
Bronchopneumonia	1*
Excessive early air leak	1
Infected segmental space—bronchial fistula	3
Total	11

Four of these 11 patients also had minor complications.
*One patient had three complications.

Transient pneumothoraces and undue retention of bronchial secretions were regarded as minor complications (Table VI). Here again, as surgical techniques and aftercare improved, the complications became less frequent.

There were no operative deaths.

TABLE VI. RESECTION FOR MINIMAL TUBERCULOSIS
MINOR POSTOPERATIVE COMPLICATIONS
119 OPERATIONS—15 COMPLICATIONS

Pneumothorax	10*
Rentention of secretions in bronchus	4
Esophagitis due to antibiotic idiosyncrasy	1

*Four patients also had serious complications.

The time which elapsed between the diagnosis of active disease and initiation of chemotherapy was relatively short. It was less than one month in 23 and between 1 and 6 months in 43. A longer interval was noted in 38 (Table VII).

TABLE VII. INITIATION OF CHEMOTHERAPY

TIME AFTER DIAGNOSIS	PATIENTS
Less than 1 month	23
1 to 6 months	43
Over 6 months	38*
Total	104

*Among these there were 9 patients with prior hospitalization and later relapse.

The concept of the therapeutic approach, the program of management, and the surgical considerations have been presented. The following section of the report is devoted to the pathologist's studies.

PATHOLOGIC STUDY

Canetti[4] has stated that: "Contrary to what is usually believed, tuberculosis is not a general disease, at least in the usual sense of the word." He further believes that the pre-eminence of local factors is clearly illustrated by several clinical facts, among them the fact "that many tuberculous patients are apparently cured by simple surgical excision of local areas."

One of the authors has independently pointed out[3, 5] that minimal pulmonary tuberculosis usually is not a part of a generalized infection but that it is a localized disease which occurs predominantly in the superior and posterior portions of pulmonary lobes. These locations are most often in upper lobes, unilateral, and more restricted in reinfection than in primary disease. While that study demonstrated a more complete picture of minimal disease, it lacked clinical and roentgenographic data for correlation with the pathologic findings.

In the present study, all cases were considered initially clinically active and at operation all palpable disease was excised. Not infrequently more disease was found at operation than was suspected from chest roentgenograms *and, on occasion, lesions were found in areas not suspected preoperatively.* In the 104 cases, a total of 119 lungs were explored and the disease excised; 89 unilateral and 15 bilateral. Because of extensive developmental bronchiectasis, a right lower lobe with some tuberculosis was removed in one case. In the remaining 118 lungs only segments or subsegments were excised. The location of the disease excised is shown in Table VIII. In only 4 lungs was there an absence of disease in the apicoposterior portion of an upper lobe or in the superior segment of a lower lobe; one of these was in the right middle lobe, one in the basal segment of a lower lobe, and 2 in the anterior segment of an upper lobe. This distribution of disease in the 119 explored lungs tallies closely with the distribution found at necropsy.[2] These findings indicate that as long as the disease remains minimal in extent roentgenologically, it is *essentially* a localized process. However, in a *few* cases, quite distant and unrecognized endobronchial disseminations may be present.

TABLE VIII. RESECTION FOR MINIMAL TUBERCULOSIS
DISTRIBUTION OF EXCISED DISEASE

SEGMENTS INVOLVED	RIGHT	LEFT	TOTALS
Apicoposterior only	39	40	79
Apicoposterior + superior	7	5	12
Apicoposterior + other	9	10	19
Superior only	1	2	3
Superior + other	–	1	1
Other not listed above	2	2	4
	58	60	118

Plus 1 lower lobe for a total of 119 resections.

The pathologic observations in the resected specimens were recorded, case by case, without reference to either the clinical record or to the type and duration of chemotherapy.

Bacteriologic examinations of the resected material were a minor feature in this study. In many instances such bacteriologic examination was deliberately kept at a minimum to allow complete morphologic studies.

Technique.—

All specimens were promptly fixed in toto, with a minimum of handling, in a 4 per cent solution of formaldehyde. Incision of the fresh specimen was restricted to the few cases in which bacteriologic culture was done. After several days' fixation, the specimens were sectioned in 4 mm. slices for the macroscopic study. From all specimens the majority of the tissue slices, and in many instances all, were processed for microscopic study. Tissue blocks were decalcified as need arose. Whenever possible, tissue blocks up to 4.5 cm. square were taken.

Several thousand random tissue sections thus became available for microscopic study and a comprehensive idea of relationships and of cellular detail was obtained.

Significant Pathologic Findings—104 Cases, 119 Lungs.—

In the prior necropsy study,[3] it was noted that with few exceptions minimal tuberculosis represented both primary and reinfection disease with primary infection predominant in the younger ages and reinfection predominant in persons beyond the fourth decade. Both primary and reinfection “minimal” tuberculosis were encountered in the group presented here.

In the study of the pathology, one lone case showed parenchymal scarring only. All other specimens showed multiple necrotic lesions and scarring but with considerable variations both in size and number of necrotic foci and amount of scar. There were considerable differences in the ages of the various types of lesions not only from case to case but within single specimens. Under these circumstances the most significant morphologic features are tabulated so as to indicate the frequency with which they were found according to cases rather *than specimens as follows:*

I. Macroscopic Features—104 Cases			
A. Multiple necrotic (caseous) lesions and parenchymal scarring			103
1. Necrotic (caseous) component dominant		83	
2. Non-necrotic component dominant		20	
a. “Tubercles” predominant	4		
b. Scarring predominant	16		
B. Evidence of cavity formation			48
1. Open		14	
2. “Filled in”		30	
3. Largely scar		4	
C. Pleural adhesions present			78
D. Calcific lesions present			37
E. Developmental bronchiectasis			7
F. Parenchymal scarring only			1
II. Microscopic Findings—104 Cases			
A. Parenchymal lesions			
1. Neutrophilic infiltration in necrotic lesions		60	
2. “Epithelioid” tubercles		53	
3. Recent pneumonic foci		10	
4. Parenchymal scarring only		1	
B. Bronchial lesions			
1. Bronchial communication with necrotic lesions		49	
2. Necrotic endobronchial tuberculosis		28	
3. Squamous metaplasia of bronchial epithelium		18	
4. Stenosis (small branches)		2	
5. Developmental bronchiectasis		7	

These data clearly indicate that a pathologic process of considerable complexity can be expected in any sizable group having clinically active minimal pulmonary tuberculosis. With such a complex pathologic process it would seem logical to regard the element of time as the most important single factor. The clinical records reveal that the lesions were removed anywhere from 4 months up to 10 years after the discovery of the disease. The pathologic picture reveals that in the majority of cases the time element is considerably longer than indicated in the clinical record. The time factor is so elusive that it becomes useless unless one dogmatically assumes that certain characteristics denote a certain age. Such personal opinion is not tenable on the basis of fact. For example, in one specimen the dominant feature may be "epithelioid" tubercles that vary in structure with the presence of only a few small well-encapsulated necrotic foci; in another, the dominant feature may be necrotic lesions of different sizes and appearances with minor parenchymal scars; in another, parenchymal scars may be dominant with only a few small innocuous appearing necrotic foci; and, in still another, there may be a fairly even mixture of all of these features. With such a variable and complex pathologic picture, it seems most difficult, if not impossible, to use a single or a combination of several morphologic features as a yardstick to determine either the duration of the time factor or the effect of any chemotherapeutic regimen.

This situation is further illustrated by the use of a single morphologic feature. It is well recognized that the endobronchial dissemination of tuberculosis requires the liquefaction and the sloughing of necrotic (caseous) lesions. In our opinion, the neutrophil through its proteolytic enzyme plays a decisive role in this process. The presence of neutrophils in necrotic lesions was noted in over one half of the cases. On the hypothesis that chemotherapy might stop the process of liquefaction, the cases were tabulated to determine whether there was a correlation between the length of time chemotherapy had been given and the amount of neutrophilic infiltration of the necrotic tissue. To show the variations found, two pairs of cases will be cited. In one pair, chemotherapy was begun promptly after the disease was discovered; in one, resection was done after 4 months of therapy and no neutrophilic infiltration of necrotic tissue was observed; in the other, resection was done after 8 months of chemotherapy and marked neutrophilic infiltration was present in several necrotic foci. In the other pair, comparable as to relationship of initiation and duration of chemotherapy, one showed no neutrophilic infiltration of necrotic tissue, while in the other the majority of the necrotic foci were considerably infiltrated with neutrophils. This difference between cases could be attributed to a difference in the manner in which an *individual* reacts to the infection. However, on several occasions, it was observed that in two closely associated necrotic lesions of similar size and macroscopic appearance one would show no evidence of neutrophilic infiltration and the other would be considerably infiltrated. The behavior of the necrotic focus, therefore, is most unpredictable and no convincing evidence has been obtained to indicate that this behavior has been radically altered by chemotherapy.

The illustrations which accompany this paper have been chosen to show several important pathologic features which the authors consider to be most relevant to the dynamics of the residual disease process after varying combinations and duration of chemotherapy. Low-power magnifications only have been used; to the clinician and the surgeon the features of relationships rather than of cellular details are of greatest significance.

Some general impressions which cannot be substantiated by morphologic data were gained from this study. The amount of clearing of roentgenographic shadows varied considerably from case to case. In some with considerable clearing, the tissue sections showed little residual scarring. It is assumed in these cases that the major portion of the pneumonic exudate in the recent endobronchial disseminations had resolved without leaving any permanent damage to the involved area. In those cases which had an insignificant amount of roentgenographic clearing, some showed a dominance of parenchymal scarring, while others showed a dominance of necrotic foci with only a small amount of scarring. From this, it would appear that extensive parenchymal scars cast roentgenographic shadows which cannot be clearly differentiated from those of necrotic lesions. In this study it would have been a correct assumption that the residual shadows were due to necrotic foci.

It was unusual to find "epithelioid" tubercles in specimens removed after more than 4 months of chemotherapy, unless there was evidence of recent liquefaction and sloughing. The "epithelioid" feature of the process seems to disappear fairly promptly under chemotherapy. From the abundant evidence of fibrosing of these tubercles, one may assume that the parenchymal scarring, so frequently encountered, represents the healed stage of "epithelioid" tubercles.

The finding of evidence of cavity formation in almost half of the cases was not anticipated. No evidence of cavity was noted in the usual posteroanterior chest roentgenograms. Planigraphy revealed suggestive evidence of cavity in six. The specimens from these 6 showed cavity formation in only one. None of the open cavities had a lumen over 5 mm. and it is not to be expected that such small cavities could be identified even by planigraphy.

Bronchial communication with a necrotic focus was found, microscopically, in 49 cases. Usually this situation was observed in a single necrotic lesion in a specimen, but in one instance such a situation was found in 4 necrotic lesions. When it is considered that several thousand sections containing numerous necrotic foci were examined, it is evident that, in tissue sections prepared in a routine manner, the finding of a bronchus opening into a necrotic focus would be infrequent. This suggests either that this phenomenon is unusual or that the opening in the necrotic lesion is difficult to locate. To investigate the latter possibility, complete serial sections were made of 4 necrotic lesions, each about 1 cm. in diameter. In each instance there was a direct bronchial opening to the zone of necrotic tissue. In each set of serial sections the bronchial connection did not extend through more than 6 consecutive sections 15 μ in thickness. Although only a few lesions were thus studied, it would seem reasonable to assume that bronchi are intimately associated with most necrotic lesions. In our opinion, this is the danger point in unsloughed necrotic lesions; it is of microscopic proportions and is difficult to locate.

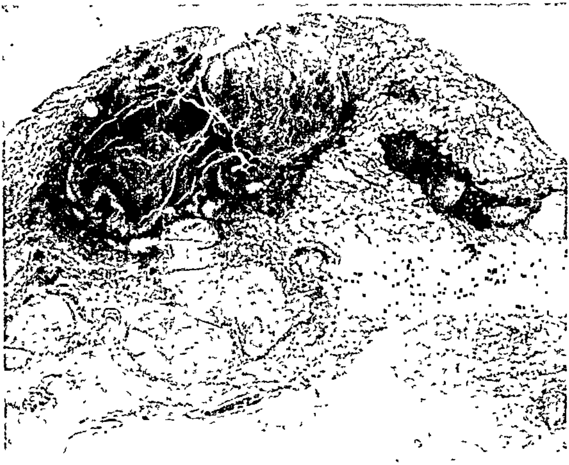

Fig 1.—White woman, age 34. Known calcified lesion at age 30. New active lesion, age 34 Sputum culture positive INH and PAS 5 months, minimal clearing. Resection, segmental plus calcified focus. Old calcified lesion, lower lobe, interpreted as obsolete focus of a primary complex.

Illustrated lesion, regarded as "exogenous reinfection," shows predominantly necrotic disease such as was present in 83 of the 104 cases Smear from large lesion was 2 plus for acid-fast bacilli; culture, negative Lesion showed some disintegration of lung tissue and neutrophilic infiltration and, in part, intact dead lung framework (elastic tissue). Other features were scattered necrotic lesions of various sizes, rare fibrosing "tubercles," and a few scars (×5; reduced ¼.)

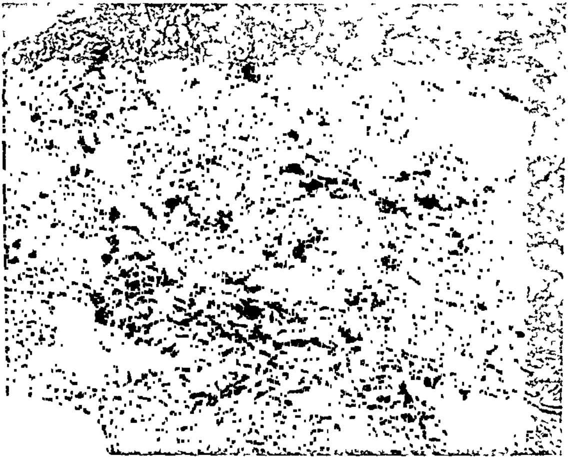

Fig 2—White woman, age 18. Diagnosis after hemoptysis Gastric cultures and tuberculin positive SM and PAS 6 months. Moderate clearing. Resection, segmental

Illustration shows parenchymal scars, the dominant feature in 16 cases. Interpreted as end stage in healing of "tubercles" A small, open, sloughing cavity was present in another area of the specimen (not shown). Calcified spot within necrotic focus, *upper right*, suggests disease of some duration; parenchymal scarring might have antedated chemotherapy. (×10; reduced ¼.)

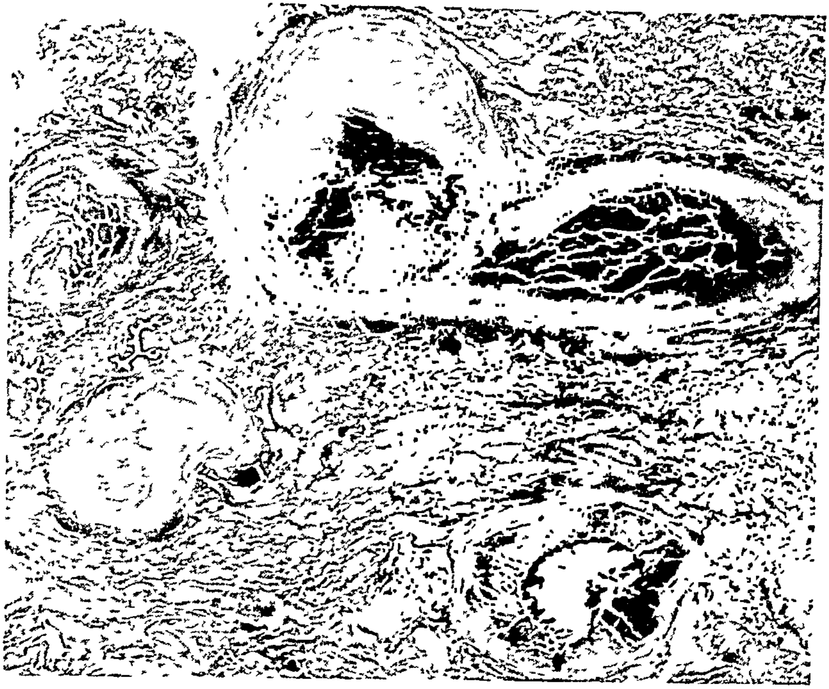

Fig 3 —White woman, age 24. Diagnosed when 6 months pregnant. Treatment started after delivery. Tuberculin positive, gastric culture positive, converted after first month SM and PAS 6 months with minor changes in roentgenograms. Resection, segmental, plus two hilar nodes.

Two areas show calcification in well-encapsulated necrosis; two other areas show neutrophilic infiltration in necrotic centers, while one necrotic area shows dead lung framework (elastic tissue). All have fibrotic peripheries. Lymph nodes showed lesions with calcification. *Interpreted as primary infection, probably of some duration.* Morphologic variations shown were encountered not infrequently. (×10; reduced 1/7)

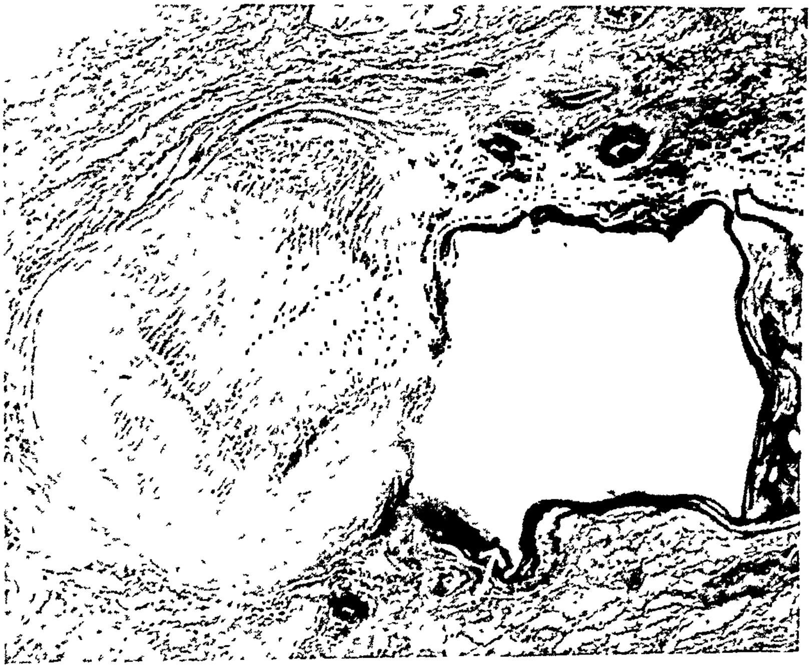

Fig. 4.—White woman, age 18. Diagnosed after negative survey films for 3 years. Tuberculin positive, gastric culture negative. SM and INH 6 *months*, moderate clearing. Segmentectomy.

Illustration shows bronchial connection with necrotic lesion. Bronchial structure to left of arrows in seat of necrotic endobronchial tuberculosis; to the right, bronchus is normal. Fibrotic periphery of lesion, *left*, well formed—acellular. (×10; reduced 1/7.)

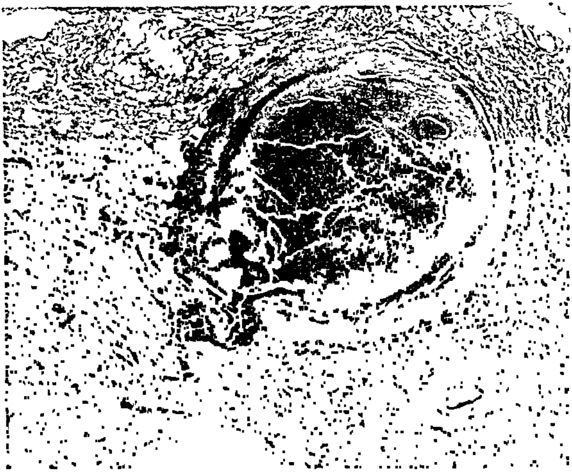

Fig. 5.—White woman, age 36. Known calcific lesion, *left lower,* 9 years. Tuberculin positive Then new lesion, *left upper.* Gastric cultures negative SM and INH 7 months, considerable clearing. Segmental resection, plus excision calcific area.

Lesion had thick, cellular fibrotic periphery and necrotic center heavily infiltrated with neutrophils Direct bronchial opening (*arrow*), stratified squamous epithelium on adjacent fibrotic wall. Bacilli present, although hard to find, in liquefying central portion. Calcified area from lower lobe apparently an obsolete primary focus. Upper lobe lesion interpreted as exogenous reinfection. (×10; reduced ¼)

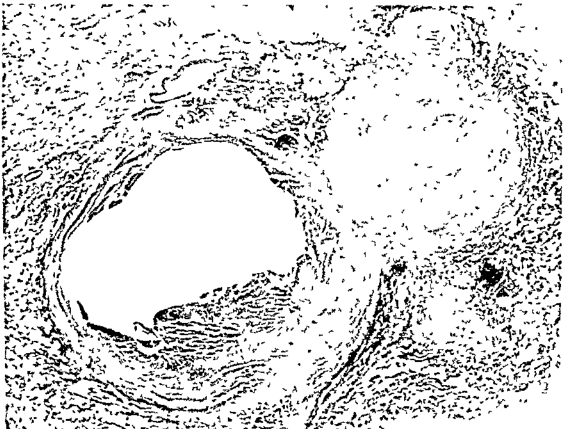

Fig 6—Same case as shown in Fig. 5

Shows small open cavity and several adjacent but separate areas of disease. Two necrotic lesions, *right upper,* have intact lung framework (elastic tissue), fibrotic peripheries more cellular than cavity-bearing lesion; they seem to be younger. Below these is an area with fibrosing tubercles, giant cells numerous Similar findings in tissue about cavity Many small colonies of acid-fast bacilli in tissue adjacent to and below cavitary hole. This of interest in view of failure to demonstrate bacilli before surgery (×10; reduced ¼)

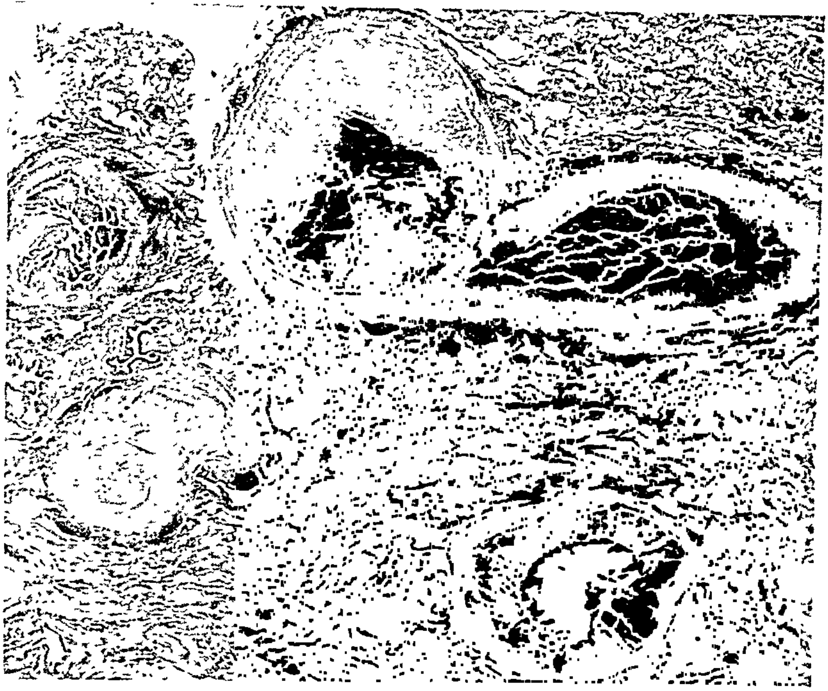

Fig. 3.—White woman, age 24. Diagnosed when 6 months pregnant. Treatment started after delivery. Tuberculin positive, gastric culture positive, converted after first month. SM and PAS 6 months with minor changes in roentgenograms. Resection, segmental, plus two hilar nodes.

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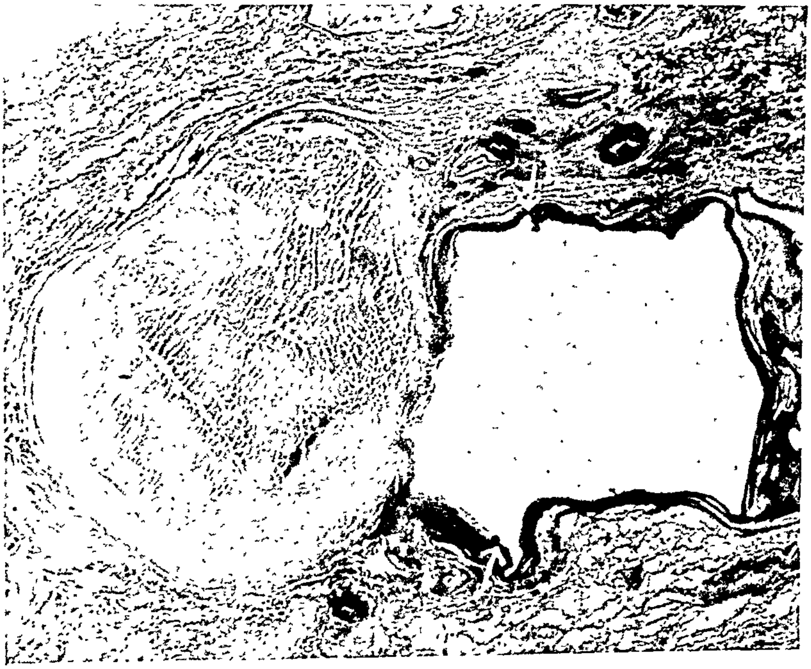

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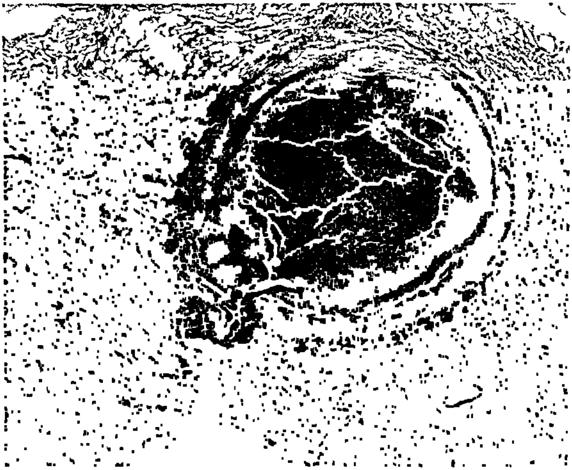

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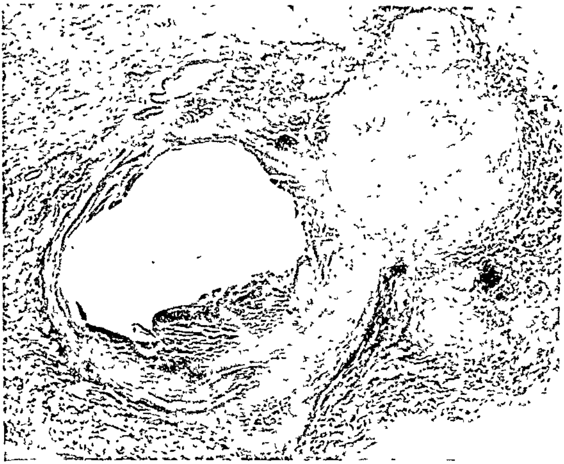

Fig 6—Same case as shown in Fig. 5

Shows small open cavity and several adjacent but separate areas of disease Two necrotic lesions, *right upper*, have intact lung framework (elastic tissue), fibrotic peripheries more cellular than cavity-bearing lesion; they seem to be younger. Below these is an area with fibrosing tubercles, giant cells numerous. Similar findings in tissue about cavity. Many small colonies of acid-fast bacilli in tissue adjacent to and below cavitary hole. This of interest in view of failure to demonstrate bacilli before surgery. (×10; reduced ⅕.)

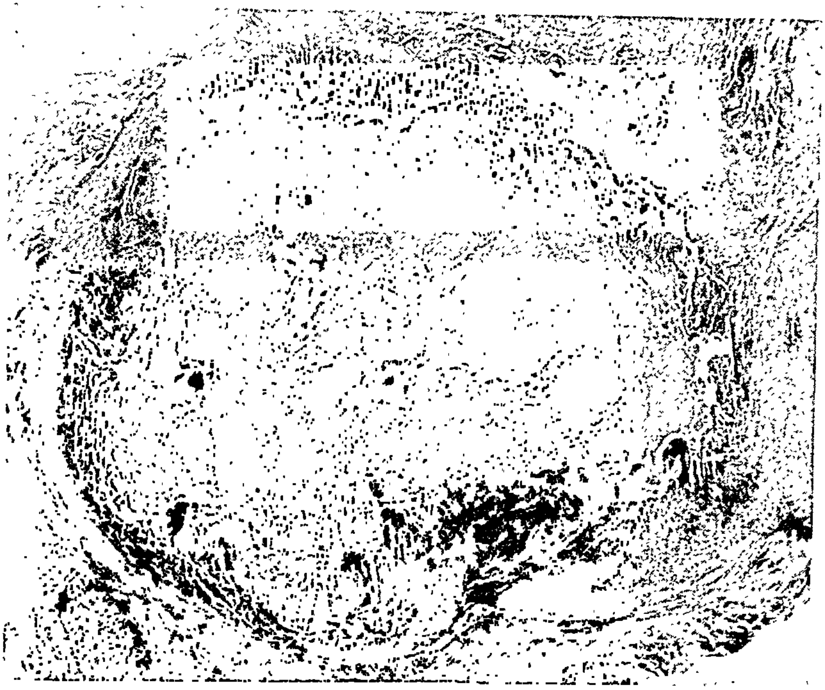

Fig. 7.—White man, age 52. Diagnosis after surgery. Sputum culture positive. SM and INH 4½ months, immediate sputum conversion. Segmentectomy.

Illustrates filled-in cavity. Necrotic contents granular. Darker peripheral zone is layer of granulation tissue with lymphocytes and monocytes but no giant cells. This represents the most common condition in which cavities were found in this study, 30 out of 48. (×10; reduced ⅓.)

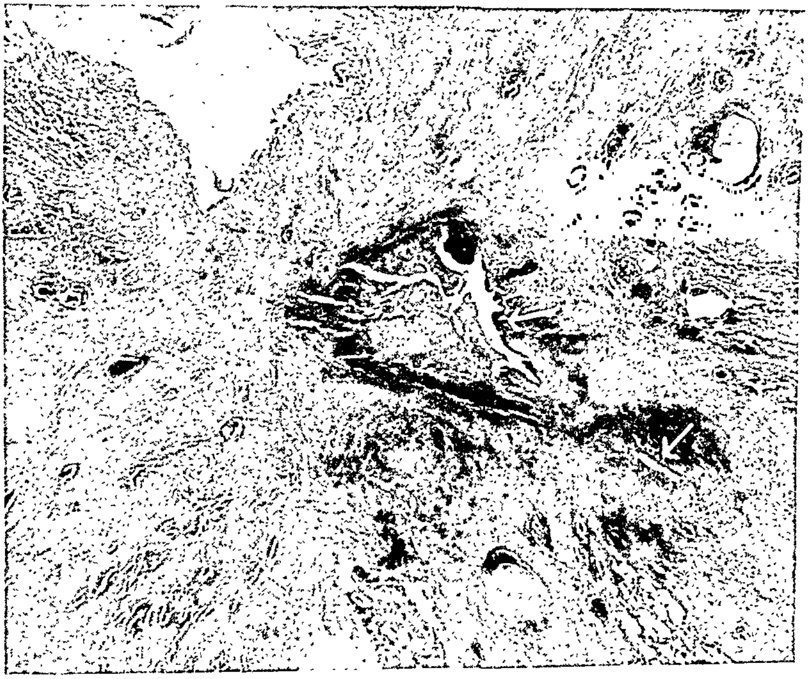

Fig. 8.—White woman, age 44. Diagnosis 1 year after "pleurisy." Sputum positive, concentrate and culture. SM and PAS 9 months (6 ambulatory), then spread. Bed rest and INH added 5 months, slight clearing. Segmentectomy.

Illustration from area of cicatrization suggesting almost complete healing of cavity, but necrotic area in center is unhealed remnant. Arrow to right shows bronchial communication. Epithelium largely squamous, a constant finding where ulcerated surface has healed. The sizable star-like scar is characteristic of cicatrizing cavities. (×10; reduced ⅓.)

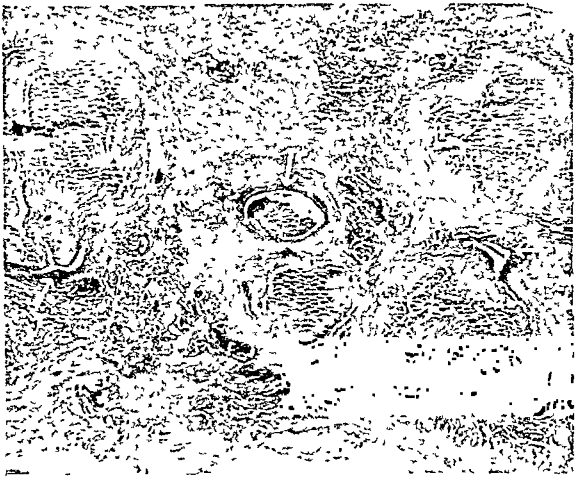

Fig. 9—Same case as shown in Fig 8

ea of "spread" shows fibrosing tubercles with giant cells, necrotic neutrophilic infiltration Arrows to right and left indicate bronchial
arrow indicates bronchus filled with neutrophilic exudate and ne-
nsive necrotic ulceration

This disease considered not over a few months old Note is made of (1) spread of disease under chemotherapy, and (2) liquefaction of necrotic lesions after 5 months of triple drug therapy (14 months total drug therapy) (X10; reduced ⅓)

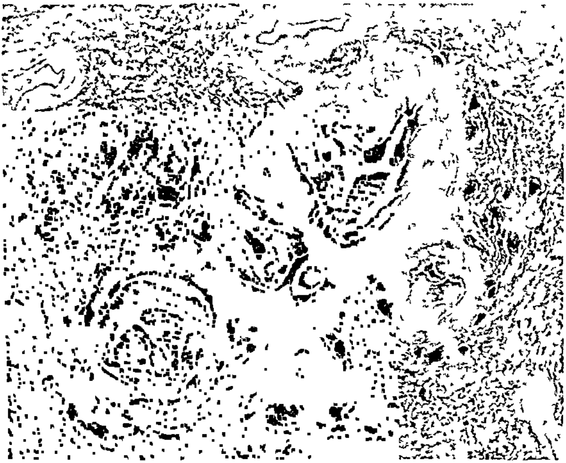

Fig 10—White woman, age 27 Diagnosis 5 years before, treated, recovery without drugs Well until 2 months before readmission, symptomatic, x-ray spread Sputum positive concentrate and culture SM and PAS 8 months Conversion after 4 months considerable clearing Segmentectomy

Illustration shows recent area of lobular pneumonia, exudate in alveolar spaces, a mixture of neutrophils monocytes, and lymphocytes Alveolar walls thickened with leukocytic infiltration No tubercles, giant cells foci of necrosis, or peripheral fibrotic zone This feature noted in 10 of the 104 evidence that small endobronchial spreads can occur during chemotherapy. (X10, reduced ⅓)

Necrotic endobronchial lesions were found frequently and were always in the smaller bronchial radicles. The ones included in the table were identified by the presence of some bronchial epithelium or small bits of cartilage. Unless some typical feature of a bronchus is noted, these lesions remain unrecognized. Stenosis of smaller bronchial branches was rarely found; in the two instances included in the table, there were necrotic endobronchial lesions in the distended bronchi distal to the stenosis.

Stratified squamous epithelial metaplasia of bronchial epithelium was noted on several occasions. This was not uniformly found at the bronchial entrance to a necrotic lesion nor at the edges of necrotic ulceration of bronchi. This phenomenon apparently occus only in those instances in which the necrotic tissue had been cleanly sloughed and a healthy granulation tissue has been produced adjacent to normal bronchial epithelium. It appears to be a constant feature whenever bronchial epithelium grows out to cover the clean granulating bed of an ulcer intimately associated with a bronchus.

COMMENT

Minimal pulmonary tuberculosis is a clinical term which connotes the roentgenographic extent of the disease. From clinical data, a patient may be considered as active or inactive and in this study only ones with active disease have been included. These cases can be divided into four categories: (a) active on the first chest roentgenogram ever taken; (b) disease of recent origin with previously normal chest roentgenograms; (c) patients who have been followed for variable periods of time and considered inactive until instability of roentgenographic shadows was observed; and (d) an increase of roentgenographic shadows in individuals who had attained an arrest of disease during a previous hospitalization. It is evident that the element of time, which considerably affects the pathologic process, varied greatly from case to case. This, in our opinion, is the situation in clinical tuberculosis as a whole.

It has long been recognized clinically that pulmonary tuberculosis runs a chronic, unpredictable course with periods of progression and regression in large numbers of patients. Likewise the value of any type of management of tuberculous patients cannot be clearly evaluated until several years have elapsed after treatment.

In the past, pathologists generally have gained their knowledge of pulmonary tuberculosis, in large part, at the necropsy table. Their chief concern has been the determination of the condition which led to the demise of the individual. Usually, a general and sketchy macroscopic description of the pulmonary situation is made and only sufficient microscopic study is done to substantiate the macroscopic diagnosis. Usually, little attention is given to a limited amount of tuberculosis of the lungs of an individual who has died from other causes. The dynamics of tuberculous disease has received little attention and commonly there is an inadequate attempt to correlate the clinical and pathologic data. Generally the work load of the pathologist is so great that time and assistance are inadequate to permit a painstaking study of the details of the dynamics of disease Everyone has had to be satisfied if a cause of death has been given These statements are made with no intent of undue criticism

These two situations were probably of little moment until it was demonstrated that chemotherapeutic agents could, in a large majority of patients, bring the tuberculosis under prompt clinical control Then the hope was voiced that, with drugs the disease could be "completely healed" At this point pathologists were asked to determine whether pathologic facts would substantiate a concept of "complete cure" When they referred back to the accumulated knowledge, they found a dearth of solid facts relating to the subtle details of the dynamics of the disease With renewed interest pathologists and bacteriologists have embarked upon intensive studies, both morphologic and bacteriologic Certain features which had not been previously documented in full were attributed to the effect of the chemotherapeutic agents without substantial proof of a cause effect relationship

The present situation is both unavoidable and unfortunate for it has led to a considerable divergence of opinion among pathologists and bacteriologists This has led to an even greater confusion relative to the use of drugs and of surgery The focal point is the necrotic (caseous) lesion, for it constitutes the major portion of the resected disease and is the major harborer of bacilli At present, most pathologists regard a well encapsulated necrotic lesion, as found in random tissue sections, as an innocuous affair even if tubercle bacilli are found within the necrotic core In our experience, lesions of this type are the most unpredictable part of the disease process A sufficient study of this portion of the pathologic process has been done to satisfy us that necrotic lesions cannot be adequately understood from random tissue sections prepared in the usual routine manner In our opinion, the delimiting zone of scar tissue that is laid down between the necrotic lesion and the surrounding healthy tissue is Nature's way of protecting the normal tissue and there is scant evidence to indicate that this function fails Of much greater .concern is the bronchial relation to, and the process of, liquefaction of the necrotic lesion From our experience, we are of the opinion that patulous bronchial communication with the necrotic pulmonary tissue is common, much more so than is generally appreciated This is the weak spot in the protective mechanism

The process of liquefaction of the dead tissue is an enigma Neutrophilic infiltration of the dead tuberculous tissue was one of the more common findings in the pathologic study of the specimens Usually it was limited to focal areas and, in the examination of different levels of a sizable lesion, the location and size of such areas were variable In our opinion, liquefaction of the necrotic tissue is induced, in large part at least, by the invasion and the proteolytic action of neutrophils If a small area of necrotic tissue is liquefied near a bronchial opening then, without demonstrable cavity formation, small dribbles can occur into the bronchus and the stage is set for new endobronchial dissemination It seems probable that the seriousness of this situation would be dependent upon the numbers of bacilli in the sloughing debris

Perhaps the most important feature of this pathologic study has been the opportunity to obtain a comprehensive survey of tuberculous disease of limited extent. Although these cases have been considered as "minimal" on clinical grounds, this diagnosis is purely arbitrary if one considers the variations in the volume of disease. Among these specimens there were found the various morphologic features which characterize tuberculous disease as a whole: from cavities which had largely, but not wholly, healed by cicatrization to those with no evidence of healing; from densely calcified or completely hyalinized necrotic lesions to those in which there was an actively forming fibrotic periphery; from early "epithelioid" tubercles without evidence of either necrosis, giant cells, or fibrosis to fibrotic ones in which only a rare giant cell was noted; from small focal areas of lobular pneumonia of such recent origin that there were no earmarks to denote tuberculous infection to abundant giant cells in some specimens and complete absence of these structures in others; and parenchymal scars of various sizes with and without lymphocytic infiltration. In some specimens practically all of the features just mentioned were found. In some specimens it was apparent that the disease must have been of considerably longer duration than suspected clinically and in others the nature of the disease would tally fairly closely with the clinical story. Under these circumstances, it would seem that caution should be used in the interpretation of morphologic features and their relationship with chemotherapy because there may be a limit to the reliability of these features as an index. The question which arises is whether Nature carries on with the reparative process, as in the era before chemotherapy, or whether chemotherapy definitely stimulates and accelerates this natural process. From the considerable variation noted between cases, it seems more logical to credit Nature with the healing or non-healing rather than to transfer such credit to the chemotherapeutic agents. One feature would seem to be undebatable: chemotherapy failed to eradicate either the necrotic tissue or the bacilli which it may harbor. This problem still remains unsolved.

This study was undertaken with two objectives considered of equal magnitude. One was to test the validity of the concept that minimal tuberculosis could be properly treated by a combination of rest and chemotherapy, followed at the appropriate time by resection surgery. The immediate results are quite satisfactory but long-term follow-up will be necessary for full evaluation. The other objective was to document the morphologic pathology in a sufficiently large series of patients so treated as to cover most, if not all, of the variants which might be expected. It is hoped that from these data the pathogenesis of minimal tuberculosis might become better understood. It is not the purpose of this study to infer that surgical removal of residual disease during chemotherapy was either a necessary or even a desirable procedure in all cases. Patients require management on the basis of the individual. The dynamics of the pathologic process should be carefully weighed while his constitution and the socioeconomic facts are under scrutiny.*

**Note:* Dr. Medlar's death and the scattering of his associates due to the closing of Biggs Hospital have left the preparation of the final draft to one of the authors. It was Dr. Medlar's aim to set forth the observations in this group of patients. He did not endeavor to correlate or reconcile his views with those of other pathologists and it would be presumptuous for a clinician or surgeon to speak for him.

Canetti[4] has pointed out the fact that pathologic material hitherto studied has been chiefly from autopsies or surgical specimens removed from patients who were not doing well. It is felt that the material reported here is a valuable supplement to prior studies in that the surgery was elective.

It may be added that Medlar had an opportunity to discuss his field of work with Canetti and that it was Medlar's feeling that they were in essential agreement. Certainly this was true of his attitude toward necrotic residues (caseum) and the fact that they are not eradicated nor their bacillary contents controlled by chemotherapy. Canetti's two concluding paragraphs include the following: (1) "As things are at present, chemotherapy cannot suffice unless the diagnosis can be established before caseation occurs." (2) "In spite of this, the important advances achieved by chemotherapy cannot be overlooked. In addition to its own effects, chemotherapy has considerably enhanced the benefits of rest, and has made surgical resection possible."

One further comment: It was Medlar's concept that as regards its necrotic component at least minimal tuberculosis is essentially a localized process. He felt that any scattered bacilli in other areas, not "protected" by necrotic (caseous) zones, would succumb to chemotherapy, and that surgical excision of the palpable necrotic foci would remove the remaining potential future threat and in effect "cure" the patient. He had even speculated that reversion to a negative tuberculin reaction might be within possibility. The validity of this thesis can only be tested by the lapse of time.

FOLLOW-UP

The health status of this group of patients following discharge from the hospital was felt to be of special interest. A consistent effort was made to secure routine follow-up observations. This has been difficult because the individuals became widely scattered. However, a significant proportion have been seen and have had at least an x-ray of the chest (Table IX).

TABLE IX. FOLLOW-UP DATA

	YEARS AFTER RESECTION					
	1	2	3	4	5	6
Patients observed: 104*	2	18	27	21	20	12
Lost to follow-up after stated year	2†	5	5	2	1†	

*No follow-up—4.
†One death each year.

Two have been lost from the group by death, one in the second postoperative year due to bronchogenic carcinoma of the opposite lung, the other in the fifth postoperative year, due to gangrene of lower extremities.

There has been one "bacteriological relapse" with a positive culture reported once in the fourth postoperative year, a finding not confirmed a month later, nor on re-examination the next year.

One clinical "relapse" occurred during the fifth year, in the lung opposite to the resection, coincident with the finding of recurrent advanced disease in the patient's wife.

SUMMARY

A study of 104 cases of minimal tuberculosis treated by rest, chemotherapy, and surgical excision is reported, together with data from pathologic studies of the resected tissue, and a follow-up report.

Bilateral surgery was performed in 15, or a total of 119 thoracotomies. No deaths resulted from the operations. Major complications occurred in 9 per cent, and were treated successfully; minor complications in 13 per cent, chiefly small temporary air leaks, were followed by full recovery.

Observations on the resected specimens are reported and discussed. The outstanding finding was the presence of necrotic lesions in 103 patients, this being the dominant feature in 83. Bronchial communication was demonstrated in 49, and believed to exist in all necrotic lesions. Cavity formation was demonstrated in 48; open in 14, "filled in" in 30, and largely scar in 4. Pneumonic foci, interpreted as recent bronchogenic spreads, were noted in 10, despite chemotherapy. There was no observed correlation between the duration of chemotherapy and the anatomic pathologic features which varied widely; nor was there a demonstrable causal relationship between chemotherapy and the observed features of the necrotic (caseous) lesions, which had not been eradicated.

The follow-up, although incomplete, gives information on 98 patients for 2 years or more, with an average of 4 years. The only known clinical relapse occurred in the fifth year.

Grateful acknowledgment is made to Dr. A. A. Zavaleta for his interest and help in this study.

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RESECTION OF ONE LOBE AND ONE SEGMENT WITH AN OSTEOPLASTIC THORACOPLASTY

Functional Results

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A COMPLICATION with infection after a pulmonary resection will reduce the function considerably. In order to avoid a postoperative infection in a remaining space, we have considered it essential to reduce the size of the thoracic cavity to fit the remaining lung parenchyma, especially in cases where such complications are frequent. Resection of one segment, in addition to a lobectomy, constitutes an absolute indication for a space-diminishing procedure. The aim of this paper is to report the functional result obtained after such resections when an osteoplastic thoracoplasty is added.

TECHNIQUE

The osteoplastic thoracoplasty is performed as easily in the face-down position as in the lateral position. The first rib may be left in place. The posterior portions of ribs 2 to 5 are resected in increasing lengths downward and fixed posteriorly by nylon sutures through drill holes in the ribs The most important technical details to prevent a herniation of the lung above the new roof are:

1. To make the second rib as short and straight as possible.
2. To incise the second costal cartilage making it possible to place the second rib close to the mediastinum.
3. The fixation of the posterior end of the second rib to the costovertebral ligament by a nylon suture.
4. The fixation of the first intercostal muscle bundle attached to the second rib to mediastinal tissue.
5. Ribs 3 to 5 are fixed by heavy catgut sutures through drill holes in the divided ribs and then pericostally around the sixth rib.

MATERIAL

Only patients with a normal contralateral lung have been selected for this postoperative study. Ten patients (8 resections on the right and 2 on the

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TABLE I. THE FUNCTIONAL RESULT OBTAINED AFTER RESECTION OF ONE LOBE AND ONE SEGMENT WITH AN OSTEOPLASTIC THORACOPLASTY

CASE	AGE	LUNG TISSUE RESECTED	OBSERVATION TIME	O_2 UPTAKE RIGHT LUNG IN % OF TOTAL	REMAINING O_2 UPTAKE OF THE OPERATED LUNG IN % OF ITS CALCULATED NORMAL VALUE	VENTILATION RIGHT LUNG IN % OF TOTAL	MAXIMAL MOVEMENTS OF DIAPHRAGM (C.M.)	
							RIGHT	LEFT
1	Woman 45	Right upper lobe + sup. segm. right lower lobe	Preop.	43	70	73		
			3 yr. postop.	23	28	35	6	7
2	Man 42	Right upper lobe + ant. basal segm. right lower lobe	Preop.	45	75	52		
			3 yr. postop.	31	41	48		
3	Man 59	Right upper lobe + sup. segm. right lower lobe	Preop.	30	40	30		
			2 yr. postop.	18	20	38	6.5	3.5
4	Woman 46	Right upper lobe + sup. segm. right lower lobe	Preop.	42	67	49		
			4 yr. postop.	41	64	48	5	6
5	Woman 30	Right upper lobe + sup. segm. right lower lobe	Preop.	49	89	57		
			4 yr. postop.	25	31	47	4.5	5
6	Woman 35	Right upper lobe + sup. segm. right lower lobe	Preop.	54	108	66		
			4 yr. postop.	45	87	60	6.5	6.5
7	Woman 34	Right lower lobe + segm. lat. middle lobe	1 yr. postop.	22	26	54	4.5	3.5
8	Woman 60	Right upper lobe + sup. segm. lower lobe + right main bronchus	Preop.	16	18	36		
			1 yr. postop.	39	59	43	4	5
9	Woman 42	Left upper lobe + sup. segm. left lower lobe	Preop.	77	32	75		
			4 yr. postop.	80	27	83	8	6
10	Man 57	Left upper lobe + sup. segm. left lower lobe	Preop.	53	96	55		
			3 yr. postop.	79	29	77	3.5	2

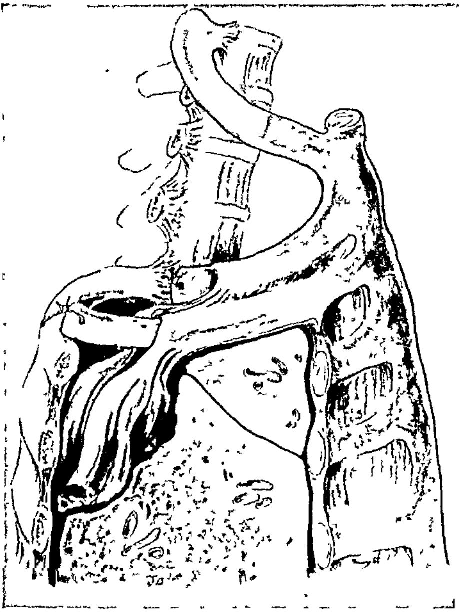

Fig 1.—Diagram of the osteoplastic thoracoplasty with resection of the posterior parts of ribs 2 to 5 with fixation of the posterior end of the rib 2 by a nylon suture through a drill hole and through the costovertebral ligament Ribs 3 to 5 are fixed by catgut sutures through drill holes and then pericostally around the sixth rib

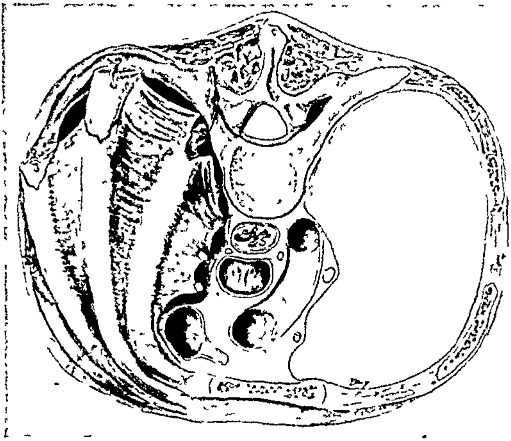

Fig. 2.—Diagram of the osteoplastic thoracoplasty as viewed from above.

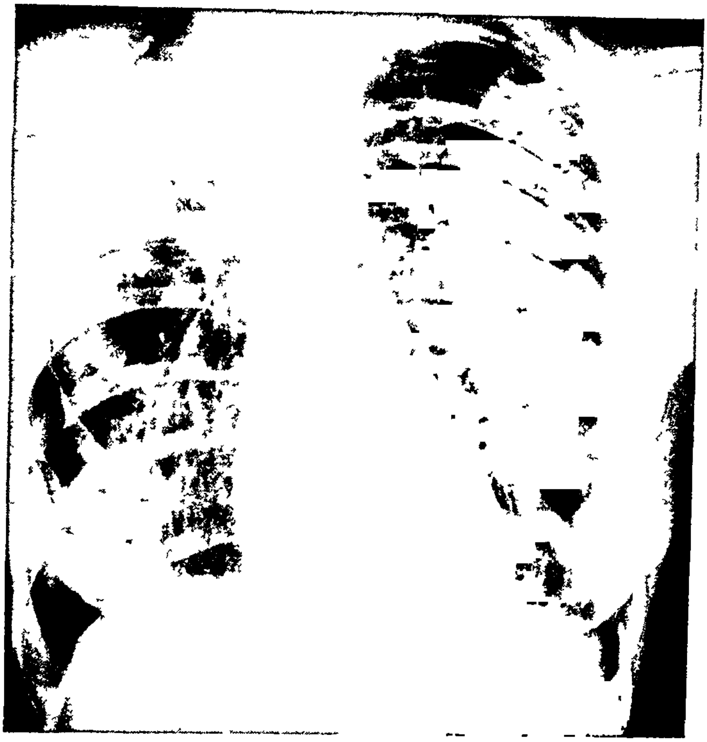

Fig 3.—Case 1 X-ray film of a 45-year-old woman taken 3 years after resection of the right upper lobe and the superior segment of the right lower lobe plus an osteoplastic thoracoplasty The patient is working full time as a housewife

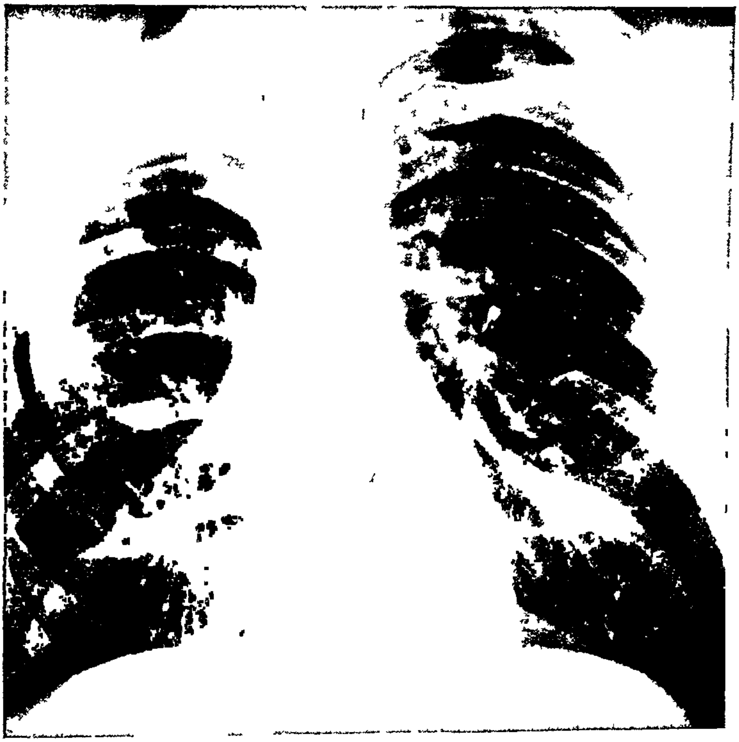

Fig 4—Case 2, a 42-year-old man X-ray film made 3 years after resection of the right upper lobe plus the anterior basal segment of the right lower lobe plus osteoplastic thoracoplasty Thirty-one per cent of the total of the oxygen uptake comes from the right lung

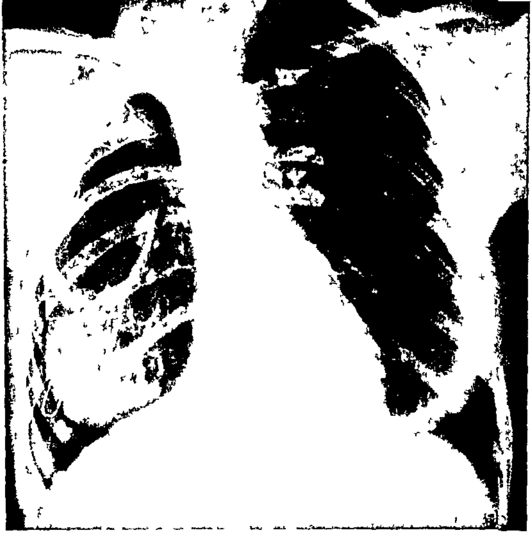

Fig 5—Case 5 a 30 year-old woman X-ray film made 4 years after resection of the right upper lobe plus the superior segment of the right lower lobe Twenty-five per cent of the total oxygen uptake comes from the right lung The patient is now working full time as a housewife

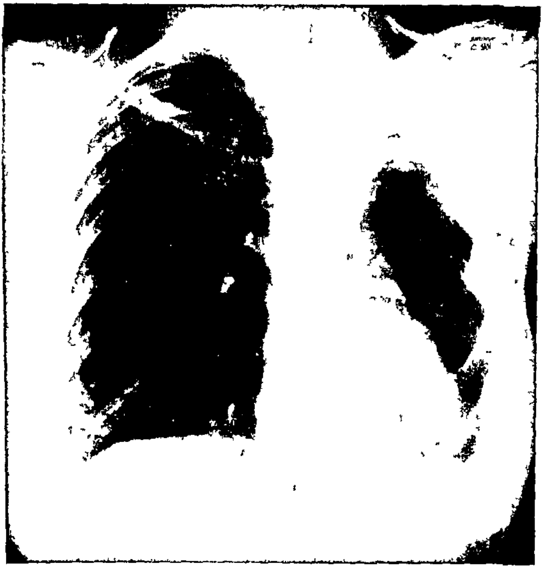

Fig 6—Case 9, a 42 year old woman X-ray film made 4 years after resection of the left upper lobe plus the superior segment of the lower lobe Twenty per cent of the total oxygen uptake now comes from the left side as compared with 23 per cent before the resection

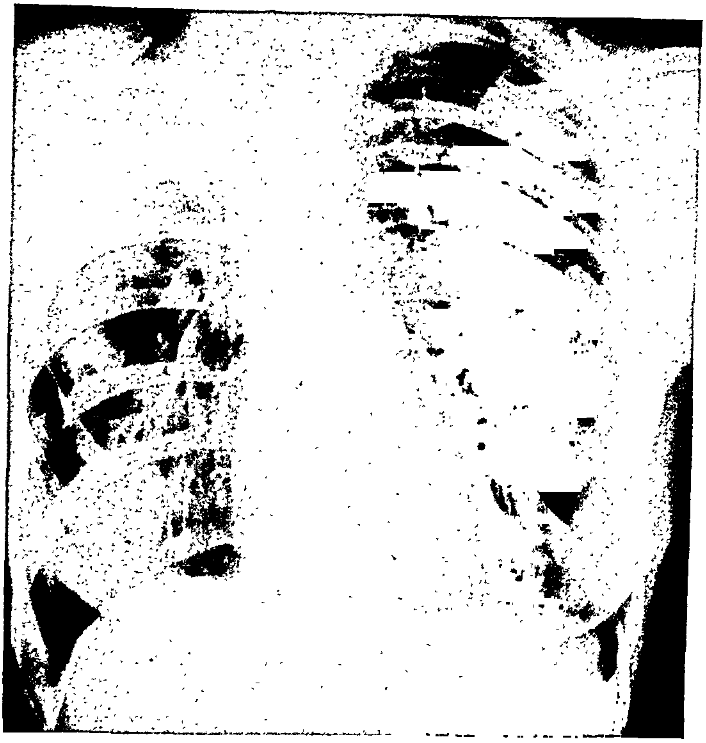

Fig. 3.—Case 1. X-ray film of a 45-year-old woman taken 3 years after resection of the right upper lobe and the superior segment of the right lower lobe plus an osteoplastic thoracoplasty. The patient is working full time as a housewife.

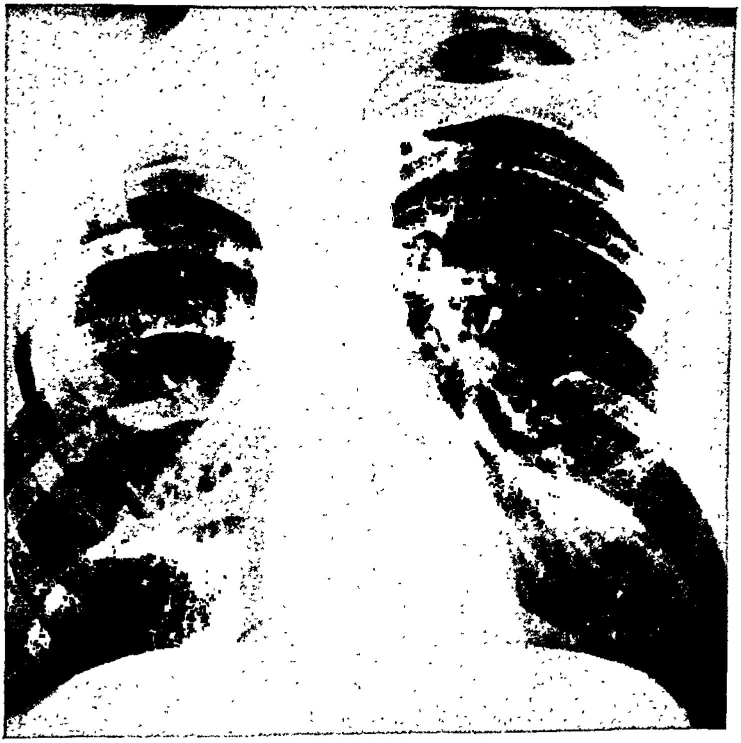

Fig. 4.—Case 2, a 42-year-old man. X-ray film made 3 years after resection of the right upper lobe plus the anterior basal segment of the right lower lobe plus osteoplastic thoracoplasty. Thirty-one per cent of the total of the oxygen uptake comes from the right lung.

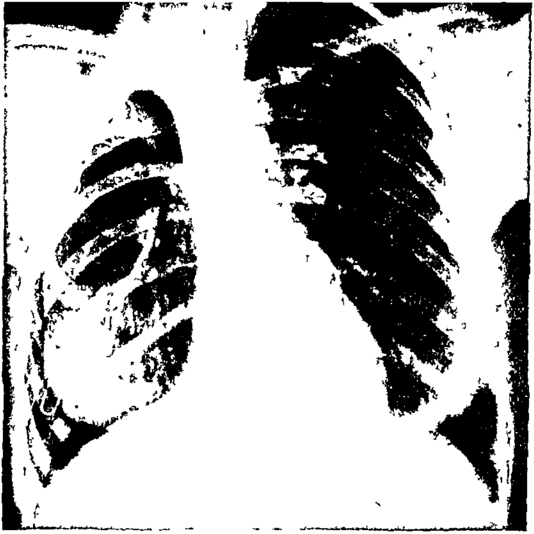

Fig 5 —Case 5 a 30-year-old woman X-ray film made 4 years after resection of the right upper lobe plus the superior segment of the right lower lobe Twenty five per cent of the total oxygen uptake comes from the right lung The patient is now working full time as a housewife

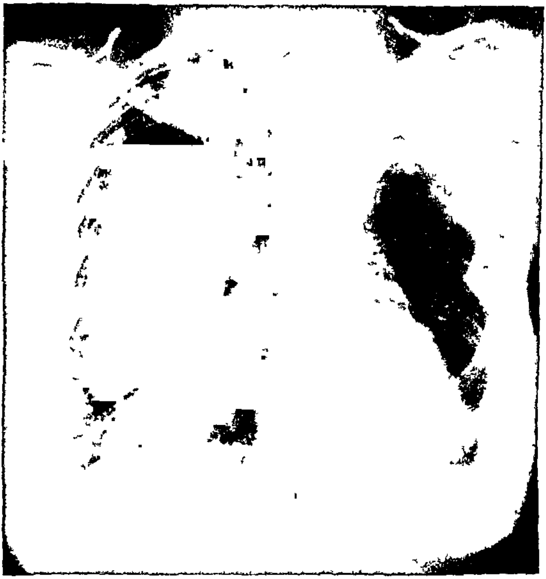

Fig 6 —Case 9, a 42 year-old woman X-ray film made 4 years after resection of the left upper lobe plus the superior segment of the lower lobe Twenty per cent of the total oxygen uptake now comes from the left side as compared with 23 per cent before the resection

left) have been followed; the function was investigated 1 to 4 years after lobectomy plus segmental resection plus osteoplastic thoracoplasty. All bronchospirometric investigations have been performed with a Carlens' double lumen catheter. The results obtained are summarized in Table I and shown in Figs. 3 to 6.

DISCUSSION

The resection of a segment in addition to one lobe will cause a further reduction of pulmonary function. Still the remaining function is good enough to recommend the continued use of the described technique. The remaining basal segments on the left side under an osteoplastic thoracoplasty has resulted in an oxygen uptake of 20 per cent of the total in 2 cases which means a remaining function of 27 per cent of the normal left lung (calculated according to Bergan):

$$\text{Reduction in per cent (right)} = 100 \times \left(1 - \frac{r \times L}{R \times l}\right).$$

l and r = per cent oxygen uptake of left and right lung after operation.

L and R = per cent oxygen uptake of left and right lung before operation.

The mean value of the oxygen uptake on the right side after the resection of one lobe and one segment under an osteoplastic thoracoplasty was 31 per cent of the total or 41 per cent of the normal right lung, calculated according to the formula just given. That value means an average decrease of 16 per cent of the oxygen uptake on the right lung for the segment resected besides the lobectomy, as the mean value in 15 cases after right upper lobectomy with osteoplastic thoracoplasty resulted in an oxygen uptake on the right side of 38 per cent of the total, or 57 per cent of the normal right lung.

Thus, the reduction in oxygen uptake after lobectomy plus segmental resection plus osteoplastic thoracoplasty on the right side was 59 per cent of the calculated normal right lung function (52 per cent of the total oxygen uptake). The mean value of the measured reduction of this operation was, in our cases, 30 per cent of the normal right lung function. The difference of 29 per cent was due to the destruction of lung tissue by disease before the operation.

SUMMARY

The functional result obtained after the resection of one lobe and one segment with an additional osteoplastic thoracoplasty is reported.

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THE EFFECT OF PULMONARY RESECTION ON THE COMPLIANCE OF HUMAN LUNGS

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INTRODUCTION

There have been several attempts to determine the effect of pulmonary resection on the elastic behavior of the lungs.[1-4] McIlroy and Bates[1] found that compliance was lower in patients following pneumonectomy than among healthy control subjects and thought the difference in elastic behavior might be important in the genesis of dyspnea. The same general observation has been made in patients undergoing less extensive surgery.[2, 3] In the study by Gliedman and his associates[3] volume-pressure measurements were made of a single lung during deflation, following distention to volumes above one liter of gas; the measurements were made while the chest was open, before and after partial resection of the same lung. Lategola and co-workers[4] found that removal of portions of the lungs from dogs altered the combined elastic behavior of the thoracic cage and lungs to an extent which depended primarily on the amount of tissue removed.

In the present study, the elastic behavior of the lungs was measured in patients during interrupted breathing, before and after resection of portions of the lungs; each patient therefore served as his own control. It was expected that changes would occur largely on the basis of a reduction in number of distensible units participating in ventilation, owing either to excision or to injury resulting from the operation. To estimate these changes in lung size, measurements were made of the total lung capacity and its subdivisions.

MATERIAL

One female and 15 male patients, all but 2 of whom had been on active duty with the armed forces, were studied. They ranged from 19 to 64 years

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From the U S Naval Hospital, St Albans, N Y

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***Present address Department of Thoracic Surgery, State University of New York, College of Medicine, Brooklyn, New York of age (mean: 33 ± 15). Their pertinent physical characteristics, diagnoses, extent of surgery, and findings in their postoperative roentgenograms of the chest are listed in Table I. With one exception, there were no serious complications during surgery or in the immediate postoperative period. The exception was Patient 10 who had a basilar empyema on the left side which required about 9 weeks to clear.

TABLE I. PHYSICAL CHARACTERISTICS AND CLINICAL DATA OF 16 PATIENTS UNDERGOING RESECTION OF LUNG TISSUE

NO.	SEX	AGE (YR.)	HT. (CM.)	B.S.A.* ($M.^2$)	DIAGNOSIS	SEGMENTS REMOVED	POSTOPERATIVE X-RAY FINDINGS	POSTOPERATIVE INTERVAL (WEEKS)
1	M	39	183	2.00	Granuloma	1	R. diaphragm elevated; r. pleural thickening along lateral wall	4
2	M	44	178	1.95	Tuberculosis	1	L. diaphragm elevated; hydropneumothorax, l. base	8
3	M	21	164	1.90	Tuberculosis	1	Minimal pleural thickening, l. upper chest	7
4	M	24	180	1.92	Granuloma	1	Minimal pleural thickening, l. upper chest	2
5	F	37	168	1.72	Granuloma	1	Minimal hydrothorax, l. base	3
6	M	22	175	1.86	Granuloma	1	Minimal pleural thickening, l. base	5
7	M	27	174	1.96	Granuloma	1	None reported	7
8	M	41	178	1.78	Bronchiectasis	2	R. diaphragm elevated; minimal pleural thickening, r. base	4
9	M	33	180	2.01	Tuberculosis	3	R. diaphragm elevated; minimal pleural thickening, r. base	8
10	M	18	175	1.81	Bronchiectasis	3	Pleural thickening, l. base	13
11	M	20	180	1.86	Bronchiectasis	4	Hydropneumothorax, l. base	8
12	M	19	183	1.97	Bronchiectasis	5	Pleural thickening, l. base	19
13	M	25	170	1.78	Bronchiectasis	6	L. diaphragm markedly elevated; pleural thickening, l. lower chest	11
14	M	21	182	1.88	Bronchiectasis	6	R. diaphragm markedly elevated; pleural thickening, r. base	9
15	M	64	175	2.08	L. bronchial ca.	8†	Mediastinal shift to left; l. lung field obscured; r. lung field normal	8
16	M	51	173	1.97	L. bronchial ca.	8†	None reported	14

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*Preoperative values for body surface area calculated from DuBois' height-weight formula: Area = $\text{weight}^{0.425} \times \text{height}^{0.725} \times 71.84$.

†Pneumonectomy (left).

METHOD

Pulmonary compliance, an index of the elastic behavior of the lungs, is the ratio of the change in volume of the lungs to the change in transpulmonary pressure.

$$\text{compliance} = \frac{\text{change in volume in liters}}{\text{change in transpulmonary pressure in cm } H_2O}$$

In human beings intraesophageal pressure is customarily measured instead of intrapleural pressure, thereby avoiding the danger of puncturing the lungs. The former measurement offers a reliable index of the pressure applied to the surface of the lungs under specified conditions.[5, 6]

The method is a modification of that used by Stead and associates[7]; it has been described previously.[8] A narrow balloon, 15 cm. long and attached to polyethylene tubing,[9] was passed through the patient's nose to the lower portion of the esophagus. The difference between pressures in the esophagus and mouthpiece was measured continuously by a pressure transducer of the inductance type.*

The patient was seated breathing air until respiration became regular. Then, at the end of normal expiration, he was connected by means of a valve to a spirometer and instructed to inspire deeply. At steps of 250 ml. (ATPS), a solenoid valve† in the inspiratory airway a few inches beyond the patient's mouth was closed automatically; the duration of valve closure varied from 1 to 2 seconds. During these interruptions of air flow, pressures equilibrated quickly throughout the lungs and upper airways so that the oral esophageal pressure difference was an index of transpulmonary pressure. Volume changes were measured with a rotational transducer attached to the wheel of the spirometer. Pressure and volume signals were amplified and recorded by a direct-writing oscillograph.‡

This technique permits measurement of changes in transpulmonary pressure during interrupted breathing at known volume increments of the lungs. When these variables are plotted on a graph, the slope of the line connecting the points gives the value for compliance. In healthy subjects, this slope is approximately rectilinear over a range of 0.75 to 1.25 L., starting from the functional residual capacity (FRC). In this paper, all values for compliance are based on measurements made during inspiration within this range of volumes.

Functional residual capacity was measured with the Darling open circuit oxygen technique; a mean value was taken of 2 measurements that agreed within 10 per cent of each other. Vital capacity (VC) was recorded on a spirometer; total lung capacity (TLC) was then calculated from the FRC and inspiratory capacity (IC). All volumes were measured with the patients lying supine and are expressed at body temperature, ambient, pressure, saturated with water vapor (BTPS).

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*Made by Mr. Frederick E. Wiedeman, 55 Shattuck Street, Boston, Mass.
†Type 8276 20, 110 volt AC, Automatic Switch Company, Orange, N. J.
‡Sanborn Co., Waltham, Mass.

Limitations of the Technique.—Measurements of pulmonary compliance are based on the assumption that gradients of pressure along the surface of the lungs are either absent or are small and remain unchanged at different stages of the respiratory cycle. Such gradients across the mediastinum or within one side of the chest would reduce the accuracy of intra-esophageal pressures (and also of intrapleural pressures obtained from a single locale) as a reflection of forces applied to the lungs. To test whether pleural pressure gradients are produced by surgery would require simultaneous bilateral pleural punctures with measurements of pressure made over large portions of both lungs, a procedure not undertaken because of its risk to the patient. Although it is likely that some inequalities of pressure did result from surgery, we have assumed that they were small. This assumption was supported in part by the fact that in the 14 patients for whom postoperative x-ray studies taken during deep inspiration were reported, the mediastinum appeared to have undergone little or no displacement; this was so even though the mediastinal structures showed little inflammatory thickening at the time of surgery and were therefore considered to be mobile. In order to reduce the possibility that measurements were affected primarily by pleural abnormalities, we have included only patients whose postoperative roentgenograms showed evidence of little or no pleural thickening. Pleural thickening as well as adhesions might influence compliance both by limiting expansion of the lungs and by creating local rigid pockets over the surface of the lungs in which the pressure would be likely to differ from that found elsewhere in the pleural space.

TABLE II. PULMONARY COMPLIANCE, END-EXPIRATORY TRANSPULMONARY PRESSURE, AND LUNG VOLUMES OF 16 PATIENTS BEFORE AND AFTER RESECTION OF LUNG TISSUE

	COMPLIANCE ($L./CM. H_2O$)		END-EXPIRATORY ESOPHAGEAL PRESSURE ($CM. H_2O$)		VITAL CAPACITY (L.)		FUNCTIONAL RESIDUAL CAPACITY (L.)		TOTAL LUNG CAPACITY (L.)	
NO.	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER	BEFORE	AFTER
1	0.18	0.08	–6.8	–7.0	4.84	3.96	3.24	2.86	7.06	5.32
2	0.12	0.14	–4.3	–4.6	4.66	4.88	3.46	2.53	7.29	6.31
3	0.14	0.12	–5.5	–8.0	4.70	4.23	2.62	2.02	6.82	5.49
4	0.21	0.20	–4.2	–5.0	5.44	4.10	2.68	2.70	6.92	5.78
5	0.19	0.19	–3.1	–5.2	4.04	2.81	2.32	—	5.62	—
6	0.19	0.19	–5.1	–4.3	4.97	3.74	2.56	2.32	6.09	5.23
7	0.22	0.18	–5.0	–3.4	5.49	—	2.48	—	6.89	—
8	0.28	0.18	–4.4	–3.5	5.48	2.82	3.34	2.99	7.80	5.33
9	0.10	0.09	–4.2	–7.1	3.88	3.18	1.79	1.57	5.25	4.17
10	0.10	0.08	–7.8	–7.9	3.34	2.73	1.86	1.63	4.36	3.13
11	0.15	0.10	–3.9	–6.7	4.62	3.20	2.45	2.54	6.11	4.94
12	0.20	0.15	–7.1	–7.7	5.25	4.23	2.68	2.52	6.36	5.78
13	0.12	0.08	–3.8	–4.6	3.51	2.55	2.24	1.88	5.25	4.02
14	0.16	0.10	–5.1	–6.3	4.15	2.80	2.77	2.62	5.56	4.34
15	0.17	0.07	–3.2	–5.4	4.07	2.35	4.28	2.28	6.80	3.70
16	0.13	0.08	–2.9	–3.7	3.93	2.07	2.00	1.28	5.48	3.11
Mean	0.166	0.127								
S.D.	0.049	0.048								

RESULTS

All values for pulmonary compliance were based on an average of 3 to 5 measurements; the factors governing variability of measurements of compliance have been described before.[8]

Individual values for compliance before and after surgery are listed in Table II Preoperatively, most of the group had values which were within a normal predicted range* The exceptions were Patients 1, 9, 10, and 13 whose compliance appeared to be significantly lowered as a result of disease

Studies were repeated from 2 to 19 weeks postoperatively (average 8 weeks) Over this period the interval between surgery and time of study bore no apparent relation to changes in compliance

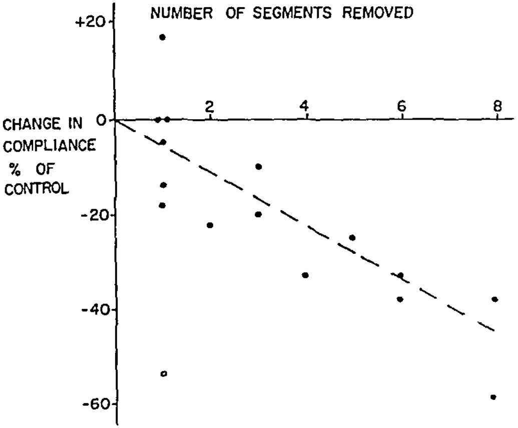

Fig 1—*Change in compliance expressed as percentage of control is plotted against number of segments removed* The broken line is the correlation that would be expected if the amount of healthy tissue contained in each segment were the same and compliance were not affected by the thoracotomy itself The measurement represented by the open circle may be an artefact (see text)

In general, there was close correlation between the fall in compliance, expressed as percentage of control values, and the number of segments of lungs removed (Fig 1) † A striking exception was Patient 7 whose compliance fell 56 per cent in spite of the removal of only one segment from the right apical lobe for a granuloma This disproportionate reduction of compliance could not be accounted for by an equivalent change in lung volume (Table II), moreover, bronchospirometric studies showed that the contribution of the right lung to total vital capacity fell only 11 per cent following surgery It is thought that the apparently sharp reduction in compliance was probably due to artefacts

Correlations were also observed when the postoperative changes (expressed again as percentages of control values) in compliance and vital capacity were

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*The statement is based on the prediction formula pulmonary compliance = 0 00343 × height 0 425 The standard deviation for such a prediction is wide however being ±0 035 L/cm H O[3]

†This correlation probably reflects the amount of healthy tiss rather number of segments removed

compared (Fig. 2), as well as when the changes in vital capacity were compared with the number of segments removed (not illustrated).

In general, the FRC was reduced and the end-expiratory transpulmonary pressures became more subatmospheric (Table II); the extent of such changes apparently did not correlate well with changes in pulmonary compliance.

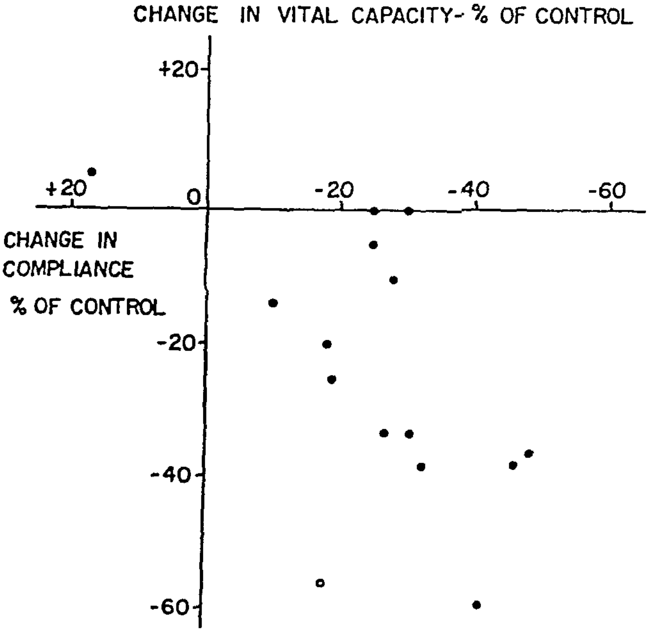

Fig. 2.—Changes in compliance and vital capacity are plotted against each other, both expressed as percentage of control. The measurement represented by the open circle may be an artefact (see text).

DISCUSSION

The patients in this study showed a reduction of pulmonary compliance roughly proportional to the amount of tissue removed. Fig. 1 compares the reduction in compliance with the change that might have been expected if, before surgery, each segment of the lungs contained an equal amount of ventilating tissue and, following surgery, there was no interference with ventilation of the remaining segments. These assumptions cannot be accepted completely. But the fact that the differences between observed and expected changes were random suggests that the thoracotomy itself had little effect on the measurement. It should be emphasized that changes in compliance were generally small compared with those seen in disabling cardiac[10-15] or granulomatous diseases of the lungs.[16] Although the data were insufficient to calculate work of breathing, it is expected to have increased significantly among patients undergoing more extensive surgery.* Because of the difficulty of evaluating disability, no attempt was made to relate it to measurements of compliance.

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*The combined flow resistance of the airways and tissues is usually greater in patients following pneumonectomy than in healthy control subjects,[1] thereby contributing to the tendency for an increase in work of breathing.

The most obvious way by which resection of tissue may affect the elastic behavior of the remaining lung is to reduce the number of units participating in ventilation In the absence of surgery, other circumstances which reduce the effective size of lungs by infiltration, collapse, or obstruction, will have a corresponding effect on pulmonary compliance Naturally, the reduction in compliance after surgery will be exaggerated if portions of the remaining lung are unable to expand because of airway obstruction, changes in mobility of the thoracic wall, or pleural reaction and thickening

Compliance is usually expressed as the ratio of changes in volume to changes in pressure in the range of tidal breathing, starting from the FRC Since these volume pressure relations vary at different levels of inflation, it is also useful to relate measurements of compliance to the total volume of gas in the lungs This has been done in Figs 3 and 4 in which the vertical axis refers to total volume of gas in the lungs and the horizontal axis refers to transpulmonary pressure, the volume at the lowest point on each curve is the FRC The ratio of the FRC to the corresponding transpulmonary pressure is an index of the over all compliance of the lungs *below* the range of volume at which spontaneous breathing occurs, that is, between the volume and pressure at end expiration and zero volume, zero pressure This ratio gives information about the elastic behavior of the lungs which is not obtained from measurement of the FRC alone Following surgery, the ratio fell among 12 of the 14 patients from whom such data were obtained (Table II), usually owing both to a decrease in FRC and an increase in distending pressure The reduction of FRC postoperatively cannot be related in a simple way to the number of segments removed, for there is evidence that the gas volume of the remaining tissue changes with time[7, 17, 19] Also, there is no reliable means of estimating to what extent the volume of individual air spaces may be modified following surgery However, if esophageal pressure is assumed to be a valid index of pleural pressure, pertinent information on changes affecting air spaces becomes available The esophageal pressure enables us to follow accurately any change in the *stress* applied to these units For example, the data of Patient 13 in Fig 3 show that transpulmonary pressure (stress applied to individual air sacs) compared at the extremes of tidal breathing was only slightly changed at the time of study following resection of 6 segments Despite the reduction in FRC postoperatively, the volume of individual units is therefore not likely to have changed significantly In general, however, it was more common for transpulmonary pressure to increase following such extensive surgery An example is Patient 14 whose data are shown in Fig 4 Before surgery, average end expiratory and end inspiratory transpulmonary pressures were 5 1 and 9 2 cm H_2O, following surgery they changed to 6 3 and 12 0 cm H_2O Had the latter pressures been applied to the intact lungs before surgery, the total volume of gas in the lungs during spontaneous breathing (on the basis of the volume pressure curve) would have ranged from approximately 3 0 to 3 9 L, rather than from the actual values of 2 8 to 3 4 L It follows that the volume of individual units also would have been greater. On the same basis, it may be assumed that postoperatively there was an increase in volume of the remaining units of tissue with respect to their volume preoperatively. To what extent the increased stress and accompanying change of volume may in time alter the mechanical function of adult human lungs is not certain. Rienhoff and his associates,[17] 6 months following pneumonectomy in dogs, could find no histologic evidence of damage to the elastic tissue or to other structural components of the alveoli. Longacre and Johansmann[18] did find a reduction in transpulmonary pressure of the remaining lung of 1 dog 4 years after pneumonectomy and concluded that the elastic recoil of the

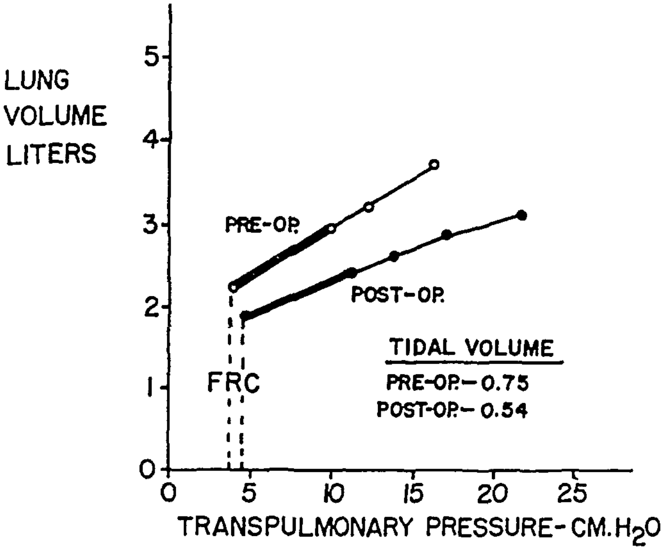

Fig. 3.—Total lung volume is plotted against transpulmonary pressure before and after resection of 6 segments. The heavy line indicates tidal volume. See text for details.

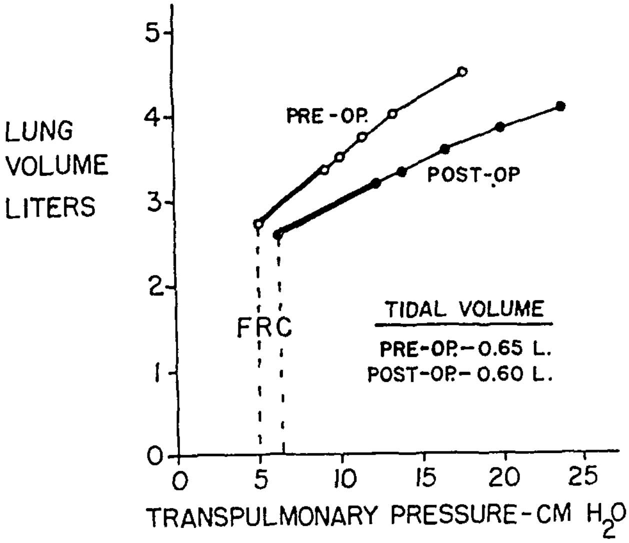

Fig. 4.—See Fig. 3.

lung had diminished. No measurements of volume were reported, although the description of the lung at autopsy suggests that its volume had increased significantly during the interval.

SUMMARY AND CONCLUSIONS

Pulmonary compliance was measured in 16 patients before and after partial resection of the lungs. The measurements were made during interrupted breathing while the patients were seated; intraesophageal pressure was used as an index of the force applied to the surface of the lungs. It was found that the pre- to postoperative change in compliance, expressed as percentage of control value, correlated closely with the number of segments of tissue removed. Almost as close was the correlation between changes in compliance and vital capacity. In general, the FRC was reduced following surgery while intraesophageal pressure became more subatmospheric. The reduction in compliance was ascribed to reduction in number of elastic units participating in ventilation.

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MALIGNANT PLEURAL MESOTHELIOMA

A Case Report With Autopsy Findings

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PRIMARY malignant tumors of mesothelial lined structures are exceedingly rare, and indeed, there is considerable controversy as to whether primary tumors of these spaces do occur. Godwin,[1] Tobiassen,[2] and McCaughey[3] have recently published comprehensive reports reviewing the literature and their personal experience with these tumors. The present report deals with a patient in whom a tumor of the parietal pleura was discovered incidentally before any symptoms ascribable to it had occurred. The tumor was already too extensive for complete removal and the patient died one year later due to widespread local growth. This case illustrates well the variation of histologic structure that can occur in malignant pleural tumors and is one more example in which the evidence appears to be conclusive that the tumor arose as a primary neoplasm in the pleural cavity. The report also contains a brief analysis of the controversy surrounding these tumors.

CASE REPORT

St. Mary's Hospital, No. 4760. A 43 year old white man was admitted to St. Mary's Hospital in September, 1955, for investigation of an abnormal shadow found on x-ray studies of the chest. Three days previously while working he had felt an acute pain in his left chest. Roentgenograms of the chest in the outpatient department revealed a vertical nonpathologic fracture of the posterior arc of the tenth left rib and a discrete shadow in the right lung field. The patient's general health had been good and except for the left chest pain he had no complaints. The family, environmental, and past history were noncontributory.

Physical examination revealed no abnormal findings except tenderness over the tenth left rib posteriorly, and a positive "spring test." Temperature, pulse, and respiration were normal. The blood pressure was 130 systolic, 80 diastolic.

Examination of the blood revealed normal values. Urine analysis was negative. Sputum culture for routine pathogens and for acid-fast bacilli, and cytologic examinations of the sputum for malignant cells were negative. Roentgenographic examination of the chest (Figs. 1 and 2), on admission showed a homogeneous shadow, 5 cm. in diameter, located peripherally in the right lung field at the level of the fourth interspace. The shadow was pyramidal in shape with a broad base peripherally. It was sharply

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demarcated. A few linear opacities were present between the shadow and the right costophrenic sinus. Bronchography and diagnostic pneumothorax showed that the shadow was not related to the bronchial tree, lung parenchyma, or visceral pleura. Bronchoscopy revealed normal findings. A gastrointestinal series, barium enema, and intravenous pyelogram revealed normal findings.

A right thoracotomy was performed through the sixth intercostal space. A sessile tumor, 5 cm. in average diameter, was found on the parietal pleura at the level of the fourth interspace in the midaxillary line. The tumor was firm, slightly movable over the underlying subpleural structures, and had a nodular surface. The visceral pleura was adherent to the surface of the tumor by fine adhesions. No mass or tumor could be palpated in the visceral pleura or in the lung. A number of small discrete nodules were present over the diaphragmatic pleura and inferior pulmonary ligament. There was no obvious lymphadenopathy. A block excision of the large tumor, together with the underlying segments of the fourth and fifth ribs, was performed. The pleural seedings were too extensive for complete removal. The postoperative course was uneventful. Review of the preoperative roentgenograms showed a small shadow in the right costophrenic sinus (Fig. 2) corresponding to the diaphragmatic nodules. The patient was discharged after 5 weeks to be followed in the outpatient department at monthly intervals.

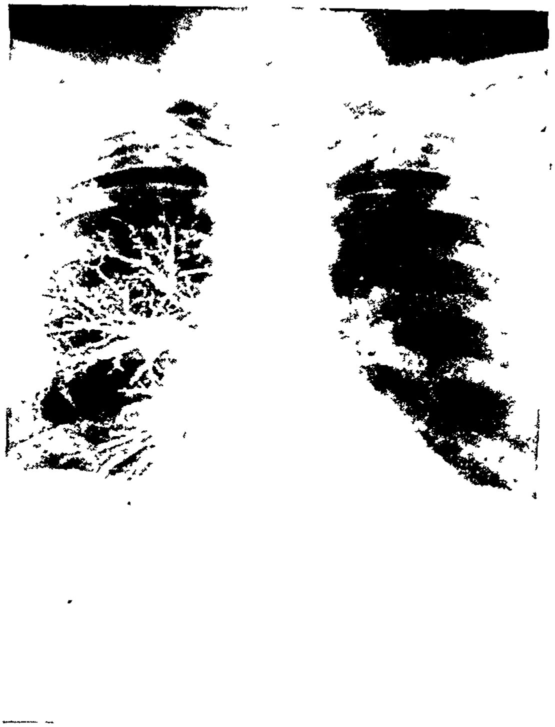


Fig. 1.

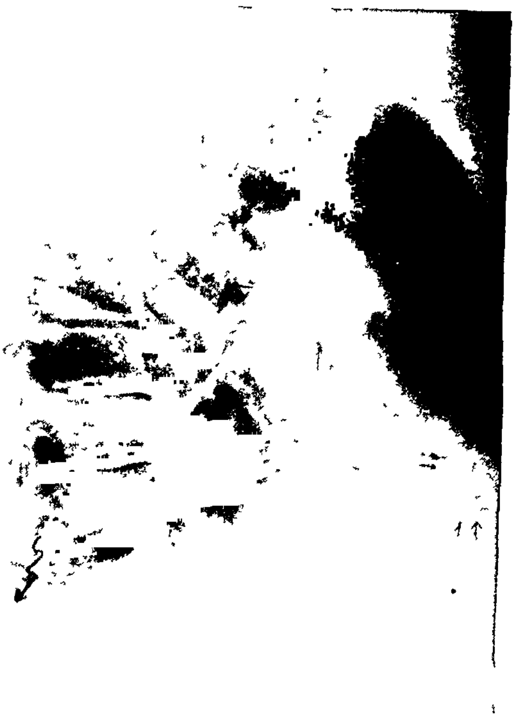


Fig. 2.

Fig. 1.—Preoperative roentgenogram of chest combined with bronchogram and diagnostic pneumothorax. The compressed right lung is outlined by the *dotted line*. A peripherally located tumor shadow is present in the right lung field. This does not follow the collapsed lung and does not distort the bronchial tree.

Fig. 2.—Preoperative lateral roentgenogram of chest. A tumor shadow is clearly seen midway between the sternum and vertebra in the mid-thorax (↗). The diaphragmatic nodules are visible in the anterior cul-de-sac (↗↗). A small amount of pleural effusion is present in the posterior cul-de-sac (↑).

He returned to work and was in good health with no complaints until August, 1956. Roentgenograms of the chest taken in July were unchanged from the postoperative films. In August, he complained of some exertional dyspnea and of stabbing pains in the midportion of the back. The pain and dyspnea gradually became more severe, necessitating readmission to hospital on Sept. 21, 1956. Physical examination revealed the patient to be poorly nourished, slightly cyanosed, and in respiratory distress. There was dullness to percussion over the entire right chest. He was afebrile, but had a rapid, irregular pulse of 160 per minute. The hemoglobin content of the blood was 16 grams per cent and the white blood count was 17,300. Roentgenograms of the chest (Fig. 3) showed a large mass occupying the lower half of the right lung field, the upper limit of which was sharply demarcated and slightly convex upward. A small pleural effusion was present in the lateral part of the right upper hemithorax. The body of the eleventh dorsal vertebra was slightly wedged, and structural changes suggested metastatic involvement. The patient's condition gradually worsened and he died on Oct. 2, 1956.

Fig. 3.—Postoperative (8 month) roentgenogram of the chest. A large tumor occupies the lower one half of the right lung field. A homogeneous shadow along the right axillary line indicates pleural effusion.

Pathologic Findings.—

1. *Surgical specimen* (S.55-1577): Two 6 cm. long segments of rib were covered on one surface by parietal pleura. From this surface a polypoid tumor, 5 cm. in average diameter, was raised 3 cm. above the level of the surrounding pleura. On cross-section (Fig. 4) the tumor appeared to be circumscribed and localized. Histologic examination showed the free surface of the tumor to be covered by dense collagen. The tumor consisted of large regular cells, with a central nucleus, and a large rim of eosinophilic cytoplasm (Fig. 5). In some areas, the cells were arranged in cords and trabeculae, in others they lined small clefts or tube-like spaces, sometimes with papillary infoldings (Fig. 6). A few of the cells contained vacuoles. The cells were supported by a loose reticular stroma. Mitotic figures were not found. The tumor, although not encapsulated, did not penetrate as far as the periosteum of the ribs and did not invade the tissues of the intercostal space. The pathologic diagnosis was mesothelioma, right parietal pleura.

2. *Autopsy* (A.56 94): (a) Gross examination: The greater portion of the right hemithorax was occupied by a large mass (Fig. 7) which was continuous with the diaphragmatic pleura and the parietal pleura of the lateral wall. In the upper part of this hemithorax, a small pleural space, containing 200 c.c. of clear fluid, remained. Small

tumor nodules were scattered over the right mediastinal pleura. The upper part of the large mass was compressed lung covered by unremarkable visceral pleura. When the mass and lung were removed, a sheet of tumor tissue was found covering the posterior parietal pleura. The lung and attached mass weighed 1,700 grams. Section through this (Fig. 8) showed the lung to be completely atelectatic and displaced toward the hilum by the tumor which measured 20 by 20 cm. There was a line of demarcation between the lung and the tumor, which did not appear to invade the lung parenchyma. No enlarged lymph nodes were found. The bronchial tree showed no tumor or ulceration. Tumor extended from the layer found on the posterior parietal pleura into the right eleventh rib and the body of the eleventh dorsal vertebra.

The left pleural cavity was free of adhesions or excess fluid. There was a healed fracture of the tenth left rib. The left lung weighed 650 grams. There was one 0.5 cm. nodule on the visceral pleura of the anterior part of the upper lobe. The parenchyma of this lung showed congestion and edema but no gross evidence of tumor. There were small gray tumor nodules scattered over the pericardial and epicardial surfaces but the pericardial sac did not contain excess fluid. The heart weighed 325 grams. Section through the epicardial nodules showed invasion into the myocardium. One nodule extended completely through the myocardium to form a small polypoid mass projecting into the left ventricle. The peritoneal cavity was normal except for a 2.5 cm. tumor nodule on the parietal peritoneum, and a smaller nodule on the serosa of the mid-jejunum. There was no other significant gross finding, although all organs were carefully examined for evidence of a small, primary tumor.

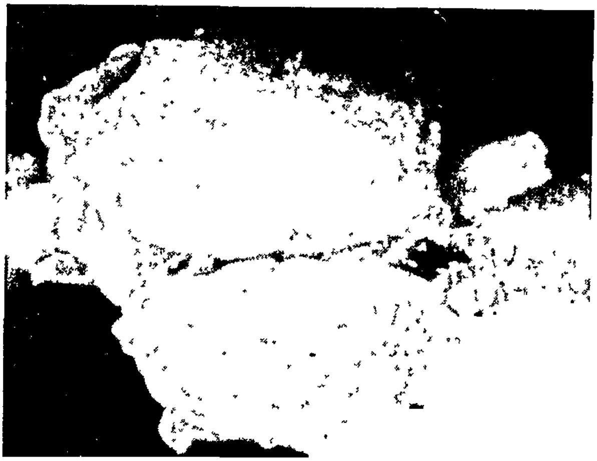
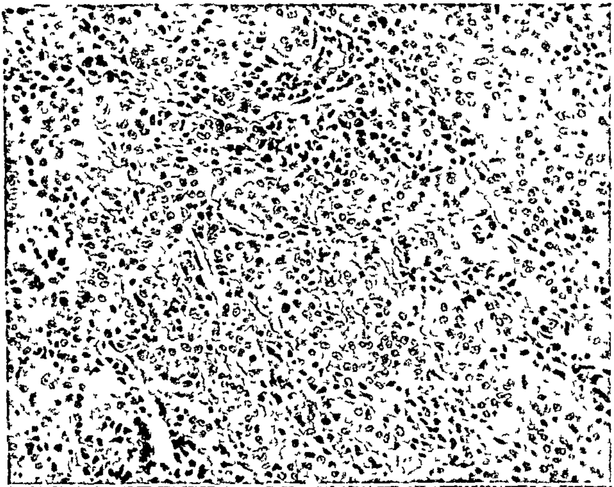


Fig. 4.—Resected tumor and rib. The tumor has been bisected showing its apparent circumscription.

(b) Microscopic findings: Tumor was present in all areas noted grossly and in addition there was a small metastatic tumor nodule in the left adrenal cortex. Tumor encased the right lung but did not appear to invade into the parenchyma. The tumor showed a basically sarcomatous pattern (Fig. 9) with fusiform cells arranged in interwoven fascicles and supported by a small amount of fine fibrillar stroma. Mitotic figures were frequent. In some areas the pattern varied, the cells being larger, less fusiform, sometimes multinucleated and occasionally vacuolated. A few areas resembled those in the surgical specimen, with cells lining clefts or tubelike spaces (Fig. 10); this pattern was found predominantly near free surfaces.

Pathological diagnosis: Diffuse mesothelioma of the right parietal pleura with extension to the right visceral and mediastinal pleura, pericardium, epicardium, myocardium, endocardium, left visceral pleura, eleventh rib, eleventh dorsal vertebrae, parietal and visceral peritoneum, and metastasis to the left adrenal gland.

Fig 5



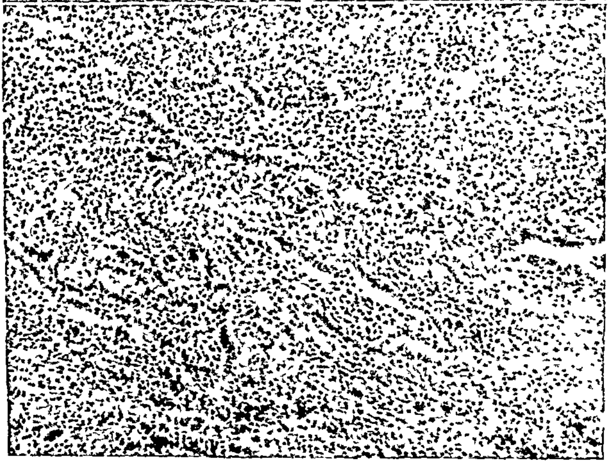


Fig 6

Fig 5.—Photomicrograph of the surgical specimen showing clefts and gland-like spaces lined by epithelium-like cells (Hematoxylin and eosin, ×100 reduced ¼)

Fig 6.—Photomicrograph of surgical specimen showing tubes of large epithelium-like cells and a few clefts (Hematoxylin and eosin, ×200, reduced ¼)

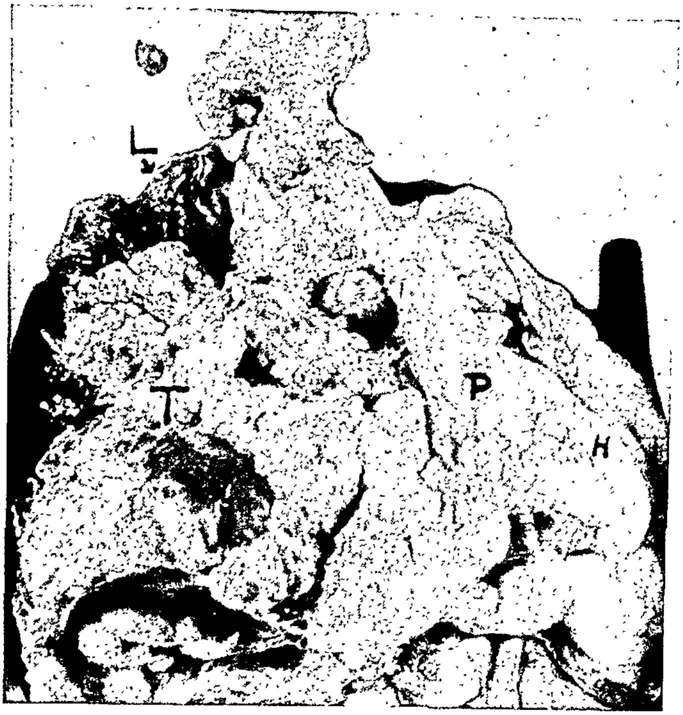


Fig. 7.—Photograph of the thoracic contents at autopsy. A large mass (*T*) occupies the major portion of the right hemithorax. The compressed right lung (*L*) is seen above this. Tumor nodules can be seen on the epicardium of the heart (*H*) and on the mediastinal pleura and pericardium (*P*).

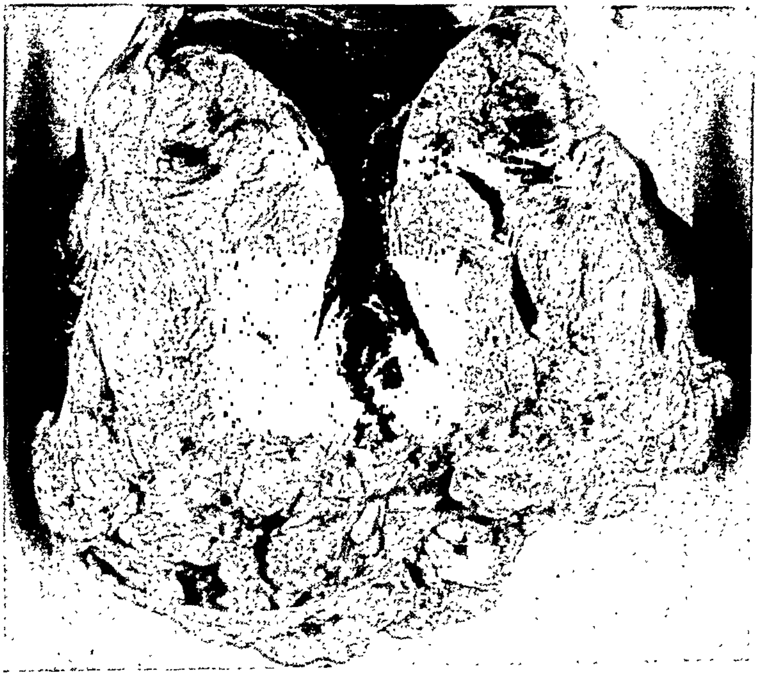
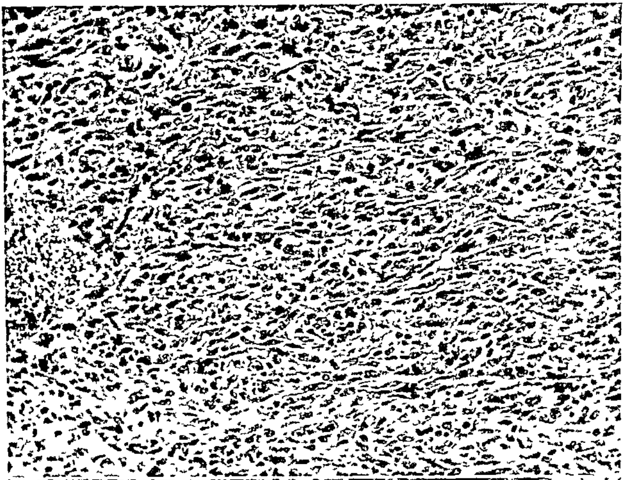


Fig. 8.—Photograph of bisected tumor mass (*T* in Fig. 7). The bisected atelectatic right lung is at the *top* and the diaphragmatic surface at the *bottom* of the photograph. There is a sharp line of demarcation between the tumor and the lung.

Fig. 9.



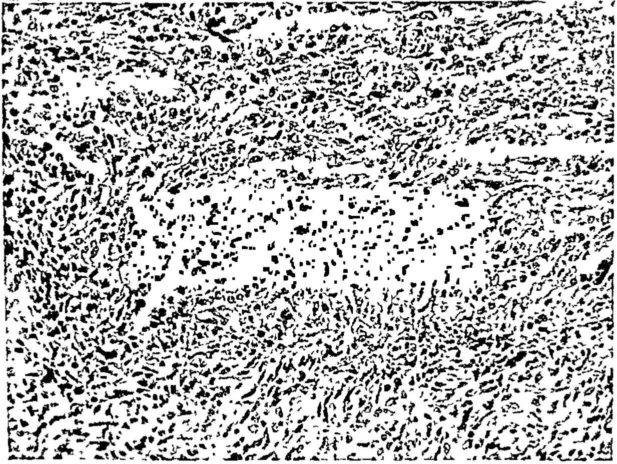


Fig 10

Fig. 9.—Photomicrograph of tumor at autopsy showing sarcomatous pattern. (Hematoxylin and eosin; ×200; reduced ¼.)

Fig. 10—Photomicrograph of tumor at autopsy. An area near a free surface in which the pattern resembled that seen in the surgical specimen (see Figs. 5 and 6). (Hematoxylin and eosin; ×200; reduced ¼.)

DISCUSSION

Stout[4] has proposed a division of primary tumors of mesothelial lined cavities into (1) a solitary fibrous variety, benign or malignant, and (2) a diffuse malignant variety. The solitary fibrous variety they described as being sharply circumscribed with the benign type being pedunculated, and the malignant type having a broad attachment to the pleura. Histologically, both subtypes of the solitary variety have a fibrous structure, the malignant type being more cellular and less differentiated. The diffuse malignant variety appears as a diffuse nodular pleural thickening which spreads widely and rapidly to invade the adjacent tissues and which may penetrate the diaphragm to invade the peritoneum. It almost never metastasizes. This variety shows a varied histologic structure. It may consist predominantly of spindle cells resembling a fibrosarcoma, predominantly of epithelium-like structure, with swollen cells arranged in cords or lining tubes, or it may consist of a mixture of the two. The fact that the localized variety may at times have a histologic structure similar to the diffuse reduces the possibility of always achieving a sharp distinction between the two groups.

The present case illustrates some of the pathologic features of the malignant variety of pleural tumors, although it is difficult to classify it as to solitary or diffuse. The surgically removed specimen gave rather a false impression of benignity. The tumor was raised above the pleural surface and seemed sharply circumscribed. Histologically, it had an epithelium-like structure with cells arranged in tubular and papillary fashion. There were no fibroblastic or sarcomatous features. At autopsy, the tumor showed a predominantly sarcomatous pattern with only rare foci of epithelium-like structure, usually in relation to free surfaces. There was widespread involvement of adjacent structures, evidence of spread through the diaphragm, and one microscopic metastatic focus in an adrenal.

The tumor was discovered incidentally before any symptoms had appeared. Combined bronchoscopy and diagnostic pneumothorax clearly demonstrated the extrapulmonary location of the lesion. In spite of this presumably early stage, the tumor had spread to the diaphragmatic pleura so that, at exploration, total removal was not considered feasible. For 9 months after operation the patient's general health remained good and chest roentgenograms showed no change; during the last 3 months of life, the tumor growth, as far as can be judged by the roentgenograms and autopsy findings, must have been extremely rapid. The cause of the changes in the growth rate of tumors is unknown.[5] The surgical procedure seems too remote to be implicated, although surgery has been accused of accelerating the rate of spread of pleural tumors. The really significant feature of these tumors is the extent of their local growth and the paucity of metastases; in the present case, although the tumor had grown into the cavity of the left ventricle, the only distant metastasis was microscopic. The poor survival rate, only months from the onset of symptoms in most cases, and the rarity of distant metastases, coupled with the failure of chemotherapy or radiation therapy to affect these tumors, indicate, we believe, that as radical a surgical procedure as technically feasible should be performed in the hope of salvaging an occasional patient. In the present case, a pleuropneumonectomy might have offered this man a better chance.

The controversy concerning the origin of pleural tumors centers around the necessity of explaining the two types of tissue, epithelial and fibrous, sometimes found in these tumors. To explain this duality, an origin from the lining layer of coelomic cavities, the mesothelium, was suggested.[6] Coelomic cavities arise from the splanchnopleure, a combination of the entoderm and splanchnic mesoderm.[7] It has been postulated that the lining layer is a separate distinct layer arising from entoderm derived cells. There is, however, a difference of opinion as to whether the lining layer in coelomic cavities is really a separate layer distinct from its supporting connective tissue. Those who feel that such a layer does exist liken it to epithelium and feel that a specific tumor can arise from it.[1-4] Those holding the opposite view believe that the lining layer merely is a flattening of the fibroblasts of the supporting connective tissue and naturally deny that any tumor can arise from what they consider to be nonexistent.[5] Embryological data and results of tissue culture studies have been cited as evidence for a distinct mesothelial layer but are far from conclusive. Experimental evidence concerning a mesothelial layer is contradictory. Williams[9] studied the healing of wounds of the peritoneum in rabbits and concluded that the lining layer re-forms from the underlying supporting connective tissue, while Cameron and his co-workers[10] studied the healing of the peritoneum in rats and felt that the lining layer regenerated from clumps of "mesothelial" cells implanted on the wound surface from the surrounding peritoneum. Experiments on the synovial membrane,[11, 12] which morphologically resembles the pleura and peritoneum, suggest that it does not have a distinct lining membrane, but that the synovial lining cells are formed from the underlying connective tissue. It would thus appear that at present there is insufficient evidence to state unequivocally whether a distinct layer, the "mesothelium" does exist in coelomic cavities. If such a layer does exist, its reaction to injury does not appear to be similar to that of the epithelium of the skin or mucous surfaces. When the lining cells of the pleura, peritoneum, or synovial membrane react to an irritant they become more numerous and assume a form which some morphologists classify as epithelial. This does not necessarily indicate embryological predeterminism, but could be related to a decrease in distorting forces so that the cells assume more nearly the circular form of free cells. It appears to be impossible to come to a firm decision on the basis of data available.

Willis[8] considers that mesotheliomata do not exist. The sarcomatous types described by Stout, he feels are ordinary fibrosarcomas and those showing epithelial structure he thinks are usually metastases from a small, undiscovered carcinoma. Although many of the reported cases may have been fibrosarcomata or metastatic carcinoma, there would now appear to be some cases which justify the conclusion that rare primary tumors which are not metastases and which have histologic features distinct from ordinary fibrosarcomata, may arise in the serous cavities. There is little doubt that the tumor reported here arose as a primary neoplasm in the pleural cavity. Careful search at autopsy failed to reveal any other possible primary site. As the tumor removed at operation had almost no fibroblastic component, consisting of cells resembling epithelial cells, and the tumor at autopsy had in the main a sarcomatous pattern with only a few epithelial-like areas, we feel that this case demonstrates clearly that the epithelial-like and sarcomatous components found in primary tumors of serosal cavities represent morphologic variations of the same neoplasm. There does not appear to be enough evidence to decide unequivocally whether these are truly primary tumors of a specialized structure, the "mesothelium," with an embryonic potential to produce both epithelial and fibrous tissue elements, or are fundamentally fibrous tissue tumors in which cells with an altered form, resembling epithelial cells, may be found. Malignant synovioma which histologically closely resemble these tumors are accepted as fundamentally sarcomatous. The term "mesothelioma" is then probably not fully justified from an academic point of view. From a practical point of view it seems to serve a purpose to denote tumors arising primarily in the serous cavities which have a varied histologic structure, and which, when malignant, have a rather uniform growth pattern with extensive invasion but with little tendency to metastasize.

SUMMARY

A case of a primary malignant tumor of the parietal pleura in a 43-year-old man is presented. A thoracotomy with removal of the main tumor was performed but diaphragmatic pleural implants precluded complete removal. The patient died one year later and autopsy showed widespread local invasion and one microscopic metastasis in an adrenal gland. Histologically, the tumor removed at operation showed an epithelium-like structure and that at autopsy mainly a sarcomatous pattern. An analysis of the controversy surrounding primary tumors of the serosal cavities is presented.

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SCALENE LYMPH NODE BIOPSY, CYTOLOGIC STUDIES, AND OTHER DIAGNOSTIC METHODS IN INTRATHORACIC DISEASE

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IN THE PAST several years, scalene lymph node biopsy has achieved general recognition as a useful adjunct in the diagnosis of intrathoracic and, at times, intra abdominal disease Following the initial report by Daniels in 1949,[1] several authors have reported their results with this technique[2-8] To date, however, only a few of these reports have included a comparison between the results of scalene node biopsy and those of exfoliative bronchial cytology in an appreciable number of cases It was, therefore, decided to carry out this comparative study, and, in addition, to review the relative effectiveness of the various techniques now commonly used in this hospital in the diagnosis of intrathoracic disease, namely x ray studies, bronchoscopy, scalene node biopsy, and exfoliative cytology When the study originally planned was completed, however, exfoliative cytology was found distinctly less useful as a diagnostic aid in this hospital than has been reported elsewhere[6, 10-14] The original review was, therefore, expanded in an attempt to explain this discrepancy It is felt that this latter part of the study may be of particular interest to those in institutions where the volume of cytologic studies does not warrant a separate subdivision of cytology in the laboratory

MATERIAL AND METHODS

All cases were reviewed from the years 1951 to 1958 in which scalene lymph node biopsy was performed and tissues were submitted to the pathology laboratory The clinical records were studied with particular attention to the pathologic diagnoses, the x ray findings, the results of bronchoscopy, the reports of any bronchial cytologic studies performed, the operative findings if thoracotomy was performed, and the final clinical diagnosis in each case Cases were included in this series only if the node biopsy was done to assist in the diagnosis of intrathoracic disease In this group, there were a few cases in which extrathoracic malignancy or other disease had been diagnosed previously, but the node biopsies were performed because the etiology of the intrathoracic disease was still in doubt Cases in which the chief complaint was enlarged cervical

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nodes or the presence of generalized lymphadenopathy of undetermined etiology were excluded. In most of the cases, the nodes removed were not palpable before operation. All cases in which tissue was submitted to the laboratory, regardless of the number of nodes identified, were included.

After selection of cases for the series by these criteria, all of the bronchial cytologic preparations that were previously reported as negative from these selected cases were reviewed. This slide review was made without knowledge as to the final clinical diagnosis in the case.

All available hospital personnel in any way concerned were then questioned as to the exact procedure they followed in the collection, transportation, or processing of the cytologic material.

RESULTS

One hundred cases of scalene lymph node biopsy were found that met the above criteria. In 62, there was a final clinical diagnosis of intrathoracic neoplasm based on a histologic study of the tissue removed at bronchoscopy, thoracotomy, or scalene node biopsy. Most of the cancers were of bronchogenic origin but a few were metastatic to the lung and scalene nodes from other sites. In the 38 noncancerous cases, there were 11 of sarcoid, 4 of tuberculosis, and 23 of miscellaneous nonneoplastic diseases.

In all of the 100 cases, there were abnormal findings in chest roentgenograms before scalene node biopsy. Depending on the location of the lesion and its lymphatic drainage,[3, 4, 15] scalene node biopsies were performed on the right side in 72 cases, on the left in 23 cases, and bilaterally in 5 cases. The pathologic diagnoses on the scalene biopsy specimens are shown in Table I. The final diagnoses in cases with negative nodes are seen in Table II. A comparison between the radiologic diagnosis and the pathologic diagnosis on the scalene node biopsy specimen from each case is seen in Table III, while a comparison between the radiologic diagnoses and final clinical diagnoses is seen in Table IV.

TABLE I. PATHOLOGIC DIAGNOSES IN 100 CASES OF SCALENE LYMPH NODE BIOPSY

NEGATIVE	MALIGNANT TUMOR	SARCOID	TUBERCULOSIS	MISCELLANEOUS
50	35	11	3	1

TABLE II. FINAL CLINICAL DIAGNOSES IN 50 CASES OF HISTOLOGICALLY NEGATIVE SCALENE LYMPH NODE BIOPSY SPECIMENS

MALIGNANT TUMOR	SARCOID	TUBERCULOSIS	MISCELLANEOUS BENIGN DISEASES
30	0	4	16

A positive diagnosis was made on examination of the lymph nodes in 50 per cent of all of the cases. For those cases in which a diagnosis of intrathoracic neoplasm was eventually established, positive scalene nodes were found in slightly more than 60 per cent of the cases.

TABLE III Correlation of Pathologic Diagnoses on Scalene Nodes With Roentgenologic Diagnoses in 96 Cases

PATHOLOGIC DIAGNOSES	ROENTGENOLOGIC DIAGNOSES			
	TUMOR	SUSPICIOUS	SARCOID	MISCELLANEOUS
Tumor	18	11	0	5
Negative	20	13	0	16
Sarcoid	2	2	1	4
Miscellaneous	1	0	0	3
Totals	41	26	1	28

TABLE IV Correlation of Roentgenologic and Final Clinical Diagnoses in 96 Cases

FINAL DIAGNOSES	ROENTGENOLOGIC DIAGNOSES			
	TUMOR	SUSPICIOUS	SARCOID	MISCELLANEOUS
Tumor	37	20	0	7
Sarcoid	2	2	1	2
Miscellaneous	2	4	0	19
Totals	41	26	1	28

Bronchoscopy was performed in 63 cases In 45 of them a histologic diagnosis of intrathoracic tumor was finally made (Table V) The bronchoscopic diagnoses used in this tabulation were those dictated in the operative note by the bronchoscopist before pathologic examination of biopsy specimens Biopsies were, however, performed at the time of bronchoscopy on all areas suspicious of neoplasm

TABLE V Correlation of Pathologic Diagnoses on Scalene Nodes With Bronchoscopic Diagnoses in 63 Cases

PATHOLOGIC DIAGNOSES	BRONCHOSCOPIC DIAGNOSES		
	NEGATIVE	SUSPICIOUS	TUMOR
Negative	13*	5†	19‡
Tumor	5	3	14
Sarcoid	2	0	1
Tuberculosis	0	0	1

*The final clinical diagnosis was tumor in 5 tuberculosis in 1 and miscellaneous in 7 cases

†The final clinical diagnosis was tumor in 2 tuberculosis in 1 and miscellaneous in 2 cases

‡The final clinical diagnosis was tumor in 16 tuberculosis in 1 and miscellaneous in 2 cases

The bronchoscopist reported the presence of tumor in almost 70 per cent of the cases of intrathoracic neoplasm, while suspicious findings were noted in an additional 10 per cent of cases On the other hand, out of 15 cases of non malignant disease, the bronchoscopist made a false positive diagnosis and reported tumor present in 3 cases with findings suspicious of tumor reported in 3 others

Papanicolaou smears were prepared in 48 of the 100 cases In one of the cases the smears were prepared only from sputum, in 3 from both sputum and bronchial aspiration or washings, and in 44 cases from bronchial aspiration or bronchial washings only

In 8 cases, the bronchial smears were reported as positive, and in all 8 cases intrathoracic tumors were present. The slides from 2 cases were considered inadequate for diagnosis. In 38 others, all smears were reported as negative, although in 27 of these 38 cases a final histologic diagnosis of intrathoracic malignancy was made.

TABLE VI. CORRELATION OF BRONCHIAL CYTOLOGIC STUDIES IN 45 CASES WITH PATHOLOGIC DIAGNOSES ON SCALENE NODES

PATHOLOGIC DIAGNOSES	CYTOLOGIC DIAGNOSES	
	NEGATIVE	TUMOR
Negative	27*	4
Tumor	10	4

*The final clinical diagnosis was tumor in 16, tuberculosis in 3, and miscellaneous in 8 cases.

Cytologic material previously reported as negative for tumor cells was available for review in 32 of these 38 cases. In the other 6 cases the smears were done at another hospital or for some other reason were not available at this time. The available smears, from 2 to 6 in number from each case, were reviewed and divided into the following 4 categories according to the quality and quantity of the cells present and the diagnosis made on those cells: (1) positive for tumor cells, 3 cases; (2) suspicious for tumor cells, but with cells too few or morphologic detail too poor to warrant a diagnosis of cancer, 10 cases; (3) no tumor cells present in a smear containing sufficient cells of good morphologic quality, 10 cases; (4) cells quantitatively or qualitatively too poor to permit a definitive diagnosis, 9 cases.

Excluding the last mentioned group of 9 cases, those in which the smears were either qualitatively or quantitatively insufficient for diagnosis, there were 23 cases in which all smears were originally called negative. Seventeen of these patients had intrathoracic neoplasms, while 6 had no neoplastic disease. On review, smears from 2 of these 17 cases were called positive, 6 cases were called suspicious, and 9 cases were called negative. In the 6 nontumor cases, the review cytologic diagnosis was positive in 1, suspicious in 4, and negative in only 1.

As noted above, 27 of the 38 cases in which smears were originally diagnosed as negative had a final histologic diagnosis of intrathoracic neoplasm. In 10 of these 27 cases, a positive diagnosis was made on the scalene node biopsy specimens.

The diagnosis of sarcoidosis was made on lymph nodes from 11 per cent of the 100 cases, a figure corresponding with that reported by others. In no case in this series did sarcoid coexist with tumor. Tuberculosis was found in one case coexisting with bronchogenic carcinoma. In this case, the specimens from bilateral scalene node biopsy were diagnosed as tuberculosis, while the diagnosis of cancer was established by bronchoscopy.

DISCUSSION

The frequency with which positive diagnoses on scalene nodes were made in this series in cases of intrathoracic neoplasm is somewhat higher than that reported by others, despite the fact that this series included all cases in which tissue was sent to the laboratory, regardless of the number of lymph nodes identified In a few cases considered as negative no nodes were identified in the submitted pad of fibro fatty tissue

The diagnostic accuracy of scalene node biopsy in different series varies from the 20 per cent reported by Wilson, Laforet, and Strieder[8] to the 48 per cent reported by Horwitz and Findlay[7] A meaningful comparison of the number or percentage of positive diagnoses in the different reported series, however, is difficult unless criteria are reported for the selection of cases for biopsy in each series Thus, where scalene lymph node biopsy is performed in cases of clinically obvious neoplastic disease, as sometimes occurs in this hospital in order to obtain histologic proof of the malignant nature and inoperability of the lesion, one would expect the percentage of positive diagnoses of neoplasm in such biopsy specimens to be quite high When, on the other hand, the scalene node biopsy is performed more or less routinely for diagnostic purposes in cases of intrathoracic disease of all types one would expect to find cancer in the pathologic specimen relatively infrequently In the series reported here, as noted under Material and Methods, the scalene node biopsies were done when an intrathoracic neoplasm was suspected Some of these biopsies were done with the thought that thoracotomy could be forestalled if a positive diagnosis of metastatic disease could be obtained by this relatively simple, although by no means completely innocuous, procedure

The study of Horwitz and Findlay demonstrates another factor that will influence the number of positive diagnoses in patients suspected of having intrathoracic cancer, namely the palpability of the supraclavicular nodes Positive biopsies were obtained in 14 of 15 cases in which nodes were palpable, while only 10 biopsy specimens contained tumor out of 29 cases in which nodes *were not* palpable[7]

It will be noted here that although bronchoscopy was performed in 63 cases, cytologic preparations of bronchial secretions or washings were made in only 47 of them In most of the 16 cases in which smears were not made, the diagnosis of neoplasm was considered fairly obvious at the time of bronchoscopy and cytologic studies were not thought necessary to establish a diagnosis The effect of this selection by the bronchoscopist, of course, was to reduce the number of cases studied cytologically in which tumor extended to, or into, the lumen of the bronchial tree and in which, presumably, exfoliated tumor cells might have been fairly numerous

The frequency of positive cytologic diagnoses reported by others in cases of bronchogenic cancer range from the 44 per cent reported by Shabart[13] to the 95 per cent reported by Foot[14] with the average diagnostic accuracy between 70 and 85 per cent

The reasons for the relatively low number of positive cytologic diagnoses, 8 of 46 cases (27 per cent), seemed to number 4 First, cells were either not exfoliated into the bronchial tree or exfoliated cells were prevented by bronchial obstruction from reaching the collection point Second, that the techniques employed in obtaining exfoliated cells from bronchial lumens were unsatisfactory

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laboratory personnel. Then too, the number of slides prepared, whether by the bronchoscopist or in the laboratory, varied from 1 to 4, with 2 the usual number. The responsibility for making this preparation was often not given to any one person and at times appropriate instructions for processing were not given to the laboratory personnel. As a consequence, there were wide differences in both the quality and the quantity of cells seen in the cytologic preparations during this 7-year period.

It is interesting to note that, despite the number of variables actually operating in the collection and processing of material from the bronchial tree, when questioned about methods most of the persons concerned with this procedure believed that fairly standardized techniques had been employed. Thus, the bronchoscopist, if he did not prepare the smear directly in the operating room, assumed that the aspirated material or the bronchial washings were being submitted to the laboratory for cytologic examination within minutes after the material was obtained. Once the aspirated material was properly tagged and the appropriate forms completed, the operating room nurse assumed that somehow the material was promptly transported to the laboratory. In actual fact, when this study was made the time lag between the operating room and the laboratory ranged from minutes to several hours. At the same time, however, laboratory personnel receiving the aspirated material assumed that the material had been brought to the laboratory immediately after being obtained.

In considering the fourth possible reason for the small number of positive smears, it is noted that the pathologist in reading the slides appears to have concerned himself primarily with the recognition of any tumor cells present. Thus, if there were no recognizable tumor cells he would report the smear as negative, despite the fact that most of the epithelial cells present may have been poorly preserved or inadequate for a definitive diagnosis. Comment may have been made on the preservation of cells but only rarely was the preparation reported as inadequate, despite the fact that 12 of the cases of intrathoracic neoplasm reviewed during this study were considered to have smears inadequate for a definitive diagnosis. If these 12 cases were eliminated from the series, then the diagnostic accuracy based on the original cytologic diagnoses would be raised from 8 out of 35 (23 per cent) to 8 out of 23 (34 per cent).

The primary reason for the disparity between the results of this cytologic study and those reported by others, then, would appear to be deficiencies in the techniques of processing the smears. Although, perhaps the best smears of bronchial aspiration or washings from all points of view are those prepared after centrifugation of freshly obtained material, the time which elapses between the bronchial aspiration and fixation is probably of greater importance than the centrifugation. When there is any possibility that more than half an hour will elapse between obtaining the specimen from the patient and fixing the material on a slide it would seem far better to have the bronchoscopist smear the aspirated material directly on slides and immerse them immediately in fixative. There may be fewer cells present in the smear than if the material had been centrifuged but, on the other hand, that material which is present will be well preserved.

If it is felt that more satisfactory cytologic preparations can be made after centrifugation of the specimen, then it would seem to be essential that a definite routine be established and that the responsibility for performing the necessary procedures be specifically assigned to one person in either the surgical or the laboratory service. Without such a designated routine, supervised by one individual, variation in procedures seems quite likely to occur *without the knowledge of either the collector of the specimen or the interpreter of the final preparation.*

Despite the rather low diagnostic accuracy of the smear in this study, 23 per cent in 35 cases of intrathoracic neoplasm, it is encouraging to note that there were only 3 cases of cancer in which negative results were obtained by bronchoscopy, cytologic studies, and lymph node biopsies. It has become almost standard procedure to perform all 3 studies at one sitting in suspected cases of intrathoracic neoplasm.

SUMMARY

One hundred consecutive cases from the years 1951 to 1958 were reviewed in which scalene node biopsy was performed as an aid in the diagnosis of intrathoracic disease. A diagnosis of tumor was made by the bronchoscopist in 70 per cent of the cases. Scalene node biopsy specimens were positive for tumor in 60 per cent of the cases when intrathoracic tumor was present. Cytologic preparations were usually made in cases which were diagnostic problems, and were not made in several cases with clinically obvious neoplastic disease. These smears contained tumor cells in only 23 per cent of the cancer cases. The relatively low diagnostic accuracy of the cystologic studies is attributed primarily to deficiencies in the techniques used in preparing the smears. On review of smears originally called negative, approximately 30 per cent were found to be insufficient for definitive diagnosis. If these inadequate smears are not considered, the diagnostic accuracy of the cytologic material becomes 34 per cent in cases of intrathoracic tumor. Each of these 3 diagnostic methods, bronchoscopy, scalene node biopsy, and cytologic study, is felt to have a definite place in the diagnostic armamentarium and each would appear to be most useful as a complemental technique rather as a replacement for the other two.

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MONILIAL EMPYEMA TREATED SUCCESSFULLY WITH INTRAPLEURAL INSTILLATIONS OF AMPHOTERICIN B

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EMPYEMA due to *Candida albicans* is an uncommon occurrence according to the literature, and effective agents for the treatment of this complication have been few. Amphotericin B recently was found to be a useful antibiotic against monilia,[1, 2, 3] and its antiyeast activity in man was reported by Childs,[4] and Halde and co-workers.[5] The fate of amphotericin B following oral, intramuscular, and intravenous administration has been described by Louria,[6] and Taylor and co-workers.[7]

The following case report concerns a patient who developed an empyema due to *Candida albicans* which was successfully treated by intrapleural instillations of amphotericin B.

CASE REPORT

A 54-year-old white man was admitted to the Francis Delafield Hospital, New York City, with the chief complaint of anterior chest pain and cough for 7 weeks. On physical examination, wheezes and rhonchi were heard over the right lower chest posteriorly, and there was clubbing of the fingers.

Significant laboratory findings showed a sedimentation rate of 60 mm. per hour, sputum smears were negative for *Mycobacterium tuberculosis* and several sputum cultures yielded only *Bacillus proteus.* Chest films revealed a cavitary mass lesion in the right lower lobe. An endoscopic biopsy from the lateral basal segmental bronchus of the right lower lobe was positive for carcinoma.

Following adequate preparation, a right pneumonectomy was performed. Examination of the specimen showed the mass in the right lower lobe to consist of undifferentiated carcinoma, and there were metastases to the tracheobronchial lymph nodes.

The patient did well after surgery until the fourteenth postoperative day, when he had a shaking chill and fever. Empyema of the right chest was diagnosed, and *Staphylococcus aureus* coagulase positive was cultured from the pleural fluid. The organism was sensitive only to chloramphenicol, novobiocin, and bacitracin. Systemic and local antibiotics were given as noted in Fig. 1, and repeated thoracenteses were performed. It became evident that the right chest could not be evacuated by needle aspiration. Two closed thoracotomies were then performed which also did not give the desired result. On the thirty-second postoperative day, an open thoracotomy was performed with the removal of all residual fluid and fibrin.

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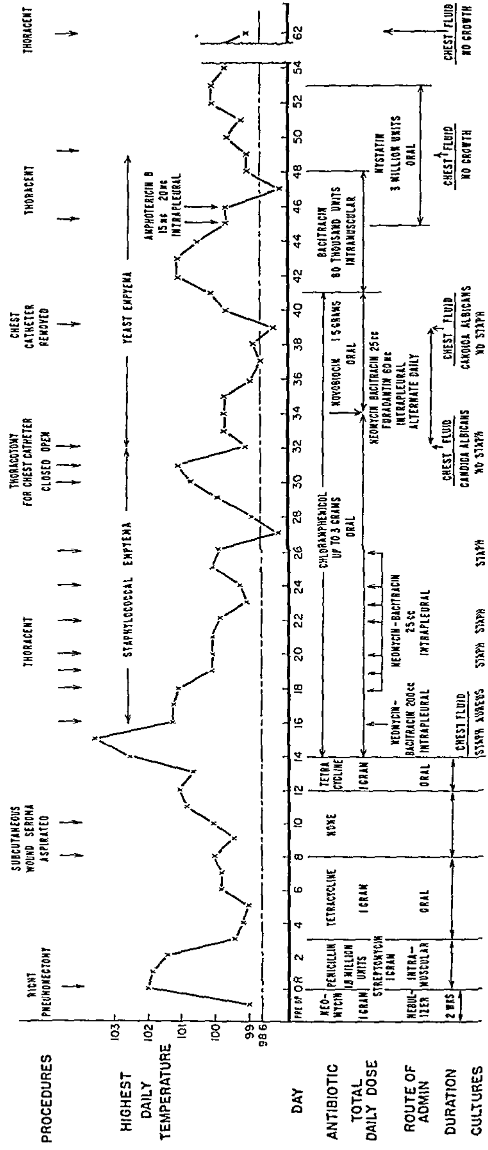

Fig 1 —Summary of clinical course and treatment given The neomycin-bacitracin solution contained 500 U/c c of bacitracin and 5 mg/c.c of neomycin

The wound was closed after a large drainage tube was inserted through a nearby interspace. Subsequent cultures were negative for *Staph. aureus*, but *C. albicans* became evident for the first time. Stool cultures also grew out this organism.

Following several days of improvement, he again developed fever. Nystatin was given by mouth to eliminate monilia from the gastrointestinal tract which was the only other known reservoir of this organism. On the forty-sixth postoperative day, 15 mg. of amphotericin B* was instilled into the pleural cavity. On the next day this treatment was repeated with 20 mg. of the drug. Following this, the patient had nausea, vomiting, malaise, pain in the right lower chest, but no fever. Fluid reaccumulated in the pleural space, but no organisms could be cultured from it after the amphotericin therapy. He was discharged from the hospital without evidence of infection.

Other significant laboratory data showed only *B. proteus* in the sputum during the entire hospital stay. Blood cultures failed to grow *C. albicans*. The patient was observed for 6 months following his discharge from the hospital, and repeated cultures were taken during this period. The blood, pleural fluid, and urine have remained sterile, and *C. albicans* was not cultured from the sputum or stool.

COMMENT

In retrospect, it would seem that *C. albicans* was introduced into the pleural cavity during one of the needle aspirations or tube insertions. When this pleural contamination was first discovered, we were not certain of its pathogenic significance. The possibility of persistent although uncultured staphylococcal infection was also entertained. Because of recurrent fever and re-collection of pleural fluid, it was decided to treat a possible bacterial empyema and a known yeast empyema. Intramuscular bacitracin was given to control the former possibility and amphotericin B was selected to treat the monilial infection.

Although intravenous amphotericin was recommended for systemic monilial infection,[6] the intrapleural route seemed to be a more direct method of treatment. Following the first intrapleural instillation, there were mild malaise and nausea. After the second injection, the patient developed severe nausea, vomiting, and chest pain. Amphotericin was discontinued, and these symptoms quickly subsided. Since the untoward reactions were so closely related to the amphotericin therapy, the concomitant nystatin and bacitracin were discounted as complicating agents. The patient's symptoms disappeared before these two agents were withdrawn. The systemic reaction indicated that there was absorption of amphotericin B from the pleural cavity although blood levels of this drug were not measured. Pleural sterilization of all organisms ultimately was achieved.

The delay of open thoracotomy on this patient may be criticized. Because the patient had known residual carcinoma in the mediastinum, it was hoped that the empyema could be cured by more conservative means. The pleural fluid was thin and turbid at all times. From this experience, it is recommended that all pleural fluid and material contaminated with *C. albicans* be evacuated from the chest followed by the instillation of amphotericin B. The use of a thoracotomy tube may be necessary. Whether a closed or open thoracotomy is used depends on the efficiency of pleural evacuation with the closed method. The removal of pleural contents must be performed under direct vision when other methods fail Following intrapleural administration of amphotericin B, the patient must be followed closely for untoward systemic reaction

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*Amphotericin B (Fungizone) was supplied by the Squibb Institute, New Brunswick, N. J.

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IDIOPATHIC MUSCULAR HYPERTROPHY OF THE ESOPHAGUS

E. L. Marston, M.D., and H. H. Bradshaw, M.D., Winston-Salem, N. C.*

IDIOPATHIC circular muscle hypertrophy of the esophagus, first described by Baillie in 1799,[1] was reviewed in 1949 by Salfelder[2] who discovered 35 autopsy cases of "esophageal hypertrophy," 4 demonstrating "idiopathic hypertrophy." Abbo and Giampalmo[3] identified 6 postmortem instances of marked degrees (0.7 to 1.1 cm.) of circular muscular hypertrophy. Sloper[1] presented 7 additional cases in 1954. Biocca[4] reviewed the literature in 1956, found 42 cases, and added 2 of his own in which surgery was performed. Sweet[5] has encountered 2 patients, Burford,[6] one, and Womack,[7] 2 patients. The following report brings the available recorded cases to 50, in 9 of which there was some form of surgical intervention.

CASE REPORT

A 51-year-old, white, married man was admitted to the hospital on Oct. 30, 1957, complaining of "stomach trouble." Twenty years prior to admission he had had substernal pain associated with nausea and vomiting. Conservative medical therapy relieved him. Subsequently he had had occasional, mild, epigastric distress, and rare, nocturnal nausea and vomiting. Three weeks prior to admission, continuous substernal pain with nausea and vomiting recurred. This distress was not related to position, meals, or activity. Hematemesis was absent. An esophagogram done elsewhere revealed an "esophageal abnormality." Dysphagia occurred for the first time 2 weeks prior to admission.

The past history revealed diphtheria in early infancy and recent mild prostatitis treated by massage.

Physical examination was normal except for a compensated anodontia and a mild prostatic enlargement. Blood pressure was 105 systolic, 60 diastolic; pulse rate 80; respirations 20; temperature 98.0° F.; weight 135 pounds.

Laboratory studies: the urine had a specific gravity of 1.023, acid, a trace of albumin, and 15 to 20 WBC's per HPF. The hemoglobin was 14.7 grams per cent and the total white count was 14,000 per milliliter, with 29 polymorphonuclears, 42 eosinophils, 1 basophil, and 28 lymphocytes. The blood urea nitrogen was 18 mg. per cent and the VDRL was nonreactive.

The chest films were normal. An esophagogram demonstrated curling of the esophagus with a delay in emptying in the distal 6 cm. The mucosal pattern was normal (Fig. 1, *A*). Esophagoscopy showed hypertrophied mucosal rugae from the 30 cm. level to the diaphragmatic pinchcock.

On Nov. 4, 1957, a left thoracotomy and mediastinal dissection exposed a firm, thickened esophagus. A frozen section from the esophageal wall was reported as benign smooth

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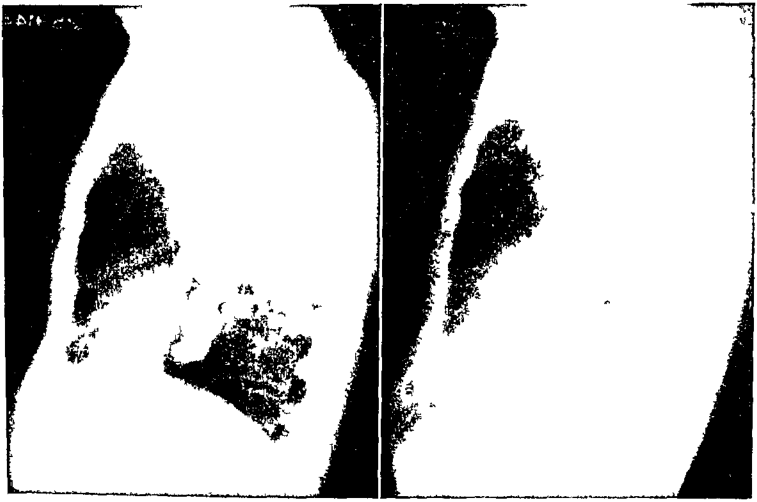
muscle An extra submucosal myotomy from the aortic arch to the gastric cardia was performed As the myotomy was performed, the mucosa and submucosa bulged outward (Fig 2) Digital exploration of the cardia, via a gastrotomy, revealed no esophageal obstruction A small sliding hiatal hernia was repaired and a routine closure performed The thoracotomy tube was removed on the third postoperative day and the Levine tube on the fourth postoperative day An esophagogram on the eighth postoperative day and on the twelfth postoperative month (Fig 1, *B*) showed mild esophageal dilatation with slight cardial delay of the barium The patient was discharged without sequelae on the ninth postoperative day Complete blood counts 3 and 12 months following surgery were normal

Microscopic examination of the circular muscle demonstrated smooth muscle hypertrophy without loss of muscular orientation An eosinophilic infiltration was present in the perivascular and perineural tissue spaces with questionable lymphangiectasis (Fig 3)



A *B*

Fig 1 — *A* Preoperative esophagogram *B* Postoperative esophagogram

ETIOLOGY

Embryologically, the circular muscle layer and myenteric plexus of Auerbach appear at 7 weeks (17 mm embryo) and the outer, longitudinal layer appears at 12 weeks (56 mm embryo) [8] There have been no reported cases in which Auerbach's plexus has been deficient

Guthrie's patient,[9] aged 11 years, is the youngest reported to date Vargas and associates[10] reported a 7 week old infant with annular hypertrophy of the cardia treated by the Heller procedure However, the average age of these patients is 60 years and tends to rule out a congenital etiology The lack of fibrosis and inflammatory exudation in the available microscopic descriptions rules out an inflammatory process

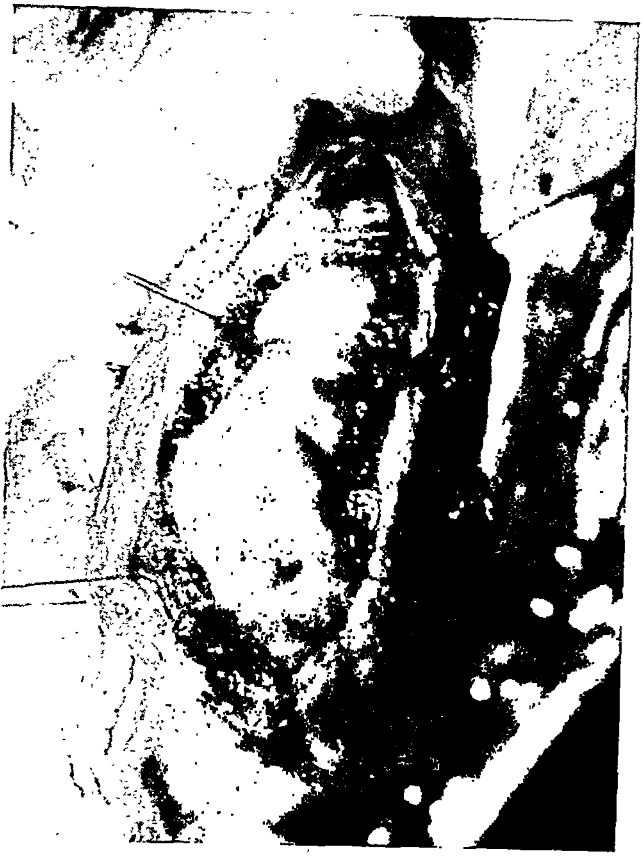


Fig. 2.—Bulging of the mucosa and submucosa at the time of surgical myotomy.

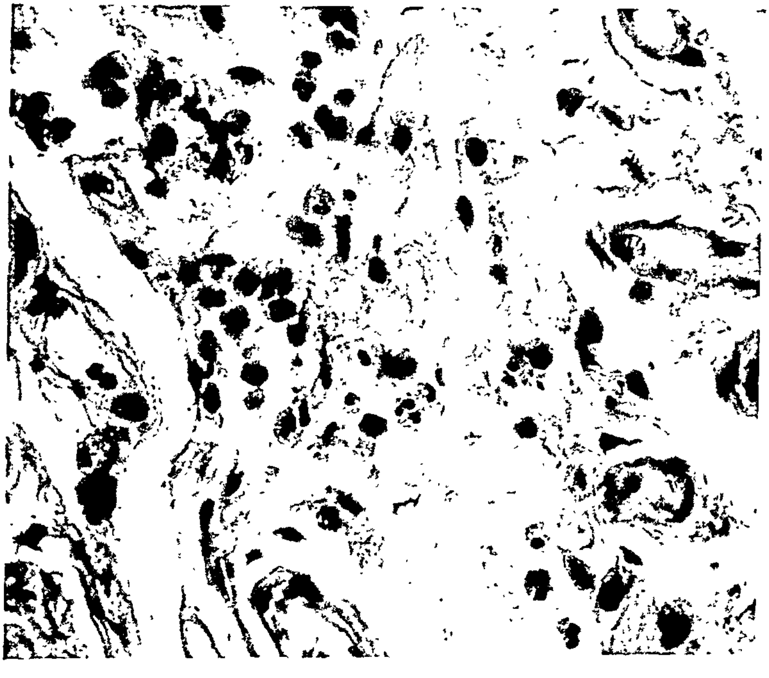


Fig. 3.—Microphotograph which demonstrates the perivascular and perilymphatic eosinophilic infiltration. (×480.)

The role of sympathetic-parasympathetic imbalance is difficult to assess Allison (cited by Sloper[1]) performed a cervical vagotomy without benefit Sympathectomy has not been performed. The frequently mentioned perineural and perivascular infiltration of eosinophils cannot be presently correlated with any known neuromuscular imbalance

The frequent occurrences of myocardial hypertrophy in these patients has suggested a humoral concept [1, 3, 4] Many of these patients are in the older age groups and have associated arteriosclerotic vascular lesions easily justifying left ventricular hypertrophy Abbo and Giampalmo[3] noted an association of pyloric hypertrophy in 7 of their 26 cases, and Sloper[1] found one in his 7 cases The incidence of malignancy in other body systems is high in these patients' protocols, Abbo and Giampalmo[3] found six malignancies in 26 cases, and Sloper[1] found five malignancies in 7 cases

The late onset of symptoms indicates that it is an acquired lesion, possibly based on an obscure allergic basis

DIAGNOSIS

Difficulty in swallowing, substernal discomfort or pain, and a history of remissions and exacerbations constitute a triad of symptoms These people learn to chew their food well before swallowing. Nausea and vomiting (not self-induced) are uncommon Patients have generally learned to live with their disease without excess distress The onset of mild to moderate substernal pain most commonly brings them to their doctor Weight loss occurs late, if at all

The barium swallow demonstrates an intact esophageal mucosa with poor peristaltic activity (although Biocca[4] reported a patient having marked activity) The barium column may hesitate at the cardia, but esophageal retention is usually not present. The esophageal lumen is not commonly stenosed Curling may be present Esophagoscopy may reveal hypertrophy of the mucosal folds or mucosal atrophy, impingement of the esophageal lumen (rare), and lack of bleeding, other than that usually encountered during esophagoscopy

PATHOLOGY

Eighty-five per cent of reported patients are male, averaging 60 years of age The hypertrophy is confined to the circular, smooth muscle layer of the esophagus The outer, longitudinal layer is not involved Rare involvement of the muscularis mucosa has been reported [3] Submucosal leiomatosis not extending into the muscularis and presenting a granular appearance has been reported [1, 3] Perivascular and perineural lymphocytic and, particularly, eosinophilic infiltrations have been frequently reported [1, 3, 4] Diffuse esophageal muscular hypertrophy and pyloric and small intestinal hypertrophy have occurred simultaneously [9]

The esophageal involvement, generally, extends from the aortic arch to the esophagogastric junction, where circular muscular hypertrophy abruptly ceases. The esophagus is firm and rubbery and the surrounding tissues are not inflamed or fibrosed.

TREATMENT

Asymptomatic patients require no therapy. Dilatations are probably of little benefit. Patients with refractory symptoms should undergo surgery. Vagotomy, as demonstrated by Allison,[1] probably has no place in therapy. Sympathectomy has not been attempted and is probably not indicated. Sweet[5] and Womack[7] performed esophagectomy on their first patients and an extra-submucosal myotomy on their second, with successful outcomes.

Allison[1] performed esophageal resection after an unsuccessful cervical vagotomy. Burford[6] and Biocca[4] performed extra-submucosal myotomies with successful results. An extra-submucosal esophageal myotomy from the aortic arch to the diaphragmatic hiatus was done with an excellent result in the patient reported here. This seems to be the surgical treatment of choice, once a malignancy has been ruled out.

SUMMARY

A 51-year-old white man, complaining of dysphagia, substernal pain, nausea and vomiting, was found to have curling of the esophagus by esophagogram, and markedly hypertrophied mucosal rugae by esophagoscopy. On a diagnosis of muscular hypertrophy, an extra-submucosal myotomy was performed with complete relief of symptoms.

Fifty similar patients have been reported. Vagotomy has been tried and found ineffective. The most effective treatment is myotomy of the esophageal muscle down to the submucosal layer, usually extending from the aortic arch to the cardia.

We wish to express our appreciation to Giuseppe Toglia, M.D., for his aid in translation of the articles from Italian medical journals.

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TRANSTHORACIC TRACHEOSTOMY

An Experimental Study

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THE STIMULUS for the present work arose from the observation of a group of 11 patients with compression of the thoracic portion of the trachea, in 3 of which a cervical tracheotomy was performed with poor or no results In 4 of these patients, the obstruction was secondary to metastatic bronchogenic carcinoma, in 2, it was due to aneurysm of the ascending portion of the aorta, and in one each of 5 to pleural mesothelioma, primary carcinoma of the trachea, Pancoast tumor, scleroma, and adenoma of the trachea All these cases were inoperable either because of the advanced stage of the disease or because of its situation in the chest, and all produced severe obstruction to the free flow of air It was thought that the only true palliation for this type of patient was an air shunt beyond the site of obstruction, therefore, the present study was undertaken in the hope that the results could be used in human beings

The review of the literature revealed that for more than 40 years there have been repeated attempts to deal with endothoracic obstruction of the trachea Thus, in 1907, Gluck[1] attempted a posterior bronchotomy but was unsuccessful Later it was conceived that the solution was in the formation of a posterior pulmonary or bronchial fistula and the following schemes were tried (a) retrograde respiration through an incision of sufficient size to reach a large bronchiole or a bronchus, (b) resection of a pulmonary lobe or a portion thereof so as to obtain the same retrograde respiration, and (c) transpleural bronchial fistula with suture of the margins of the skin to the walls of the open bronchus Kuttner,[2] in 1908, operated on a patient with compression of the trachea produced by an aortic aneurysm, this author resected the upper lobe and fixed the open bronchus to the skin but the patient died a few days later In 1922, Rethi Pest[3] published a report of a case of a pulmonary fistula performed in two operations in a patient with aortic aneurysm who survived 14 months and 12 days with an adequate respiratory exchange through the fistula In the same year, Knasek[4] attempted a posterior bronchotomy following Gluck's technique but unfortunately the patient died the next day With the exception of Rethi Pest's case, all other attempts were unsuccessful

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Other means to relieve the obstruction of the trachea were suggested by Guleke.[5] Following the decompressive mediastinotomy, described in 1897 by Milton,[6] this same procedure has also been supported more recently by Abbott[7] who has emphasized the fact that several weeks must elapse after the procedure before the patient can appreciate the beneficial results. Sloan and Cowley[8] published, in 1951, a report of a case of aortic aneurysm with severe compression of the trachea in which they performed a posterior mediastinal tracheotomy by means of a rubber tube; the patient died 4 months later with rupture of the aneurysm but throughout the postoperative period the tracheotomy functioned adequately. The authors stress the necessity of constant aspiration of the artificial airway, as well as intense treatment with antibiotics since secretions are abundant and easily become infected. In 1942, Watson[9] reported a case of primary carcinoma of the trachea with resection of the involved segment and anastomosis of the cephalic end to a skin tube with an opening practiced beforehand in the sternum. Kleitsch[10] performed a tracheotomy in a case of recurrent carcinoma of the larynx and opened the trachea to the skin by means of a polyethylene tube at the level of the sternum; this author insists on the convenience of the anterior access because the patient can look after the stoma and sleep in a dorsal position. A similar case was reported by Minor[11] who anastomosed the trachea to the sternum; both authors emphasized the importance of keeping the new respiratory tract patent by means of repeated aspirations and of the uninterrupted use of antibiotics.

We have also attempted the transthoracic tracheotomy with a rubber tube after Sloan and Cowley[8] in a case of low tracheal obstruction but the patient was lost in the operating room because of unsurmountable technical problems.

The only published experimental wo   e by Minkin[12] who, in 1925,
performed transpleural bronchotomy ir   is work cont   iled
descriptions of the surgical access and t   e operation   a
transverse bronchotomy in situ after an   removal
and fifth ribs; the br   pening is a   infundi
with the skin. The   vival wa   e cause o
always empyema.

EXPERIMENTAL

Forty-six dogs,   15   ope
anastomosing the tho   lat   t
chest. In 32 of these   e   d,
sections were examined
were carried out in 18.

The animals were an
ether-oxygen mixture; indu
In all cases, a right thorac
during the operation, blood
Antibiotics were used postope

Variations in surgical technique permit separation of our animals in the following three groups: Group 1—complete endothoracic tracheostomy, 23 dogs; Group 2—partial endothoracic tracheostomy with a polyethylene tube, 18 dogs; and Group 3—partial endothoracic tracheostomy with a polyethylene tube covered by skin, 5 dogs

RESULTS

Group 1. Complete Endothoracic Tracheostomy.—

After opening the thorax and resecting the fifth rib in the usual manner, the trachea is dissected in its endothoracic portion as high as possible, fixed by means of two separate sutures in the cartilaginous portion, and an opening is made in the membranous portion immediately beneath the two sutures. The upper end is closed with separate sutures and simultaneously the lower end is connected with the anesthetic tube in order to continue the pulmonary insufflation (Fig 1). The azygos vein is sectioned in order to permit a greater mobility to the pulmonary hilus.

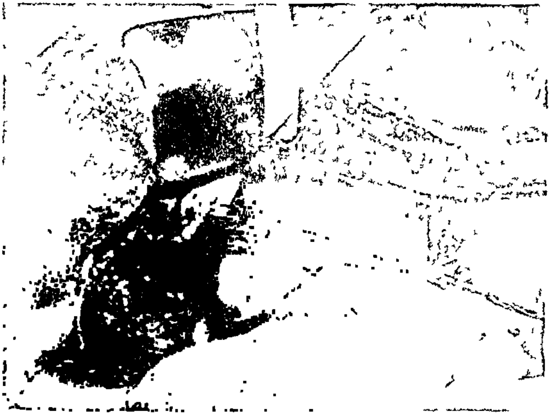

Fig 1—Complete tracheostomy Observe the anesthetic tube introduced in the lower portion of the trachea and the suture of the upper half of the trachea

The free end of the lower portion of the trachea is fixed to the wall of the thorax by suturing it to each one of the different planes in order to ensure a permanent position in the parietal course (Fig. 2). Twenty-three dogs were operated upon using the previous technique and they all died in periods ranging from 7 hours (Dog 30) to 14 days (Dog 29). Autopsies were performed in 18, histologic study of lungs and trachea in 14, and bacteriologic studies of tracheal and bronchial secretions in 11. In all animals succumbing after 24 hours or less, there were no clinical manifestations of obstruction and death was attributed to the operation since the respiratory exchange was adequate. In all animals dying after 24 hours of the operation, the predominant clinical picture was progressive dyspnea and tracheobronchitis ending in bronchopneumonia. Autopsy was performed with special interest in the contents of the tracheobronchial tree, the lungs, and the relation of the trachea with the wall of the chest. In the tracheocutaneous juncture, there were inflammatory and infectious changes while in the tracheobronchial tree there was a whole range of changes from slight to purulent tracheitis and intense bronchopneumonia. The

Fig. 2.—Comr Notice t

histologic exa he g
were alpha *Str us,*
sp., Micrococcus re
which are habit
of these germs was
Pseudomonas aerugi
related to the survival

Group 2.—Partial

thorax was op
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abou
ous

an

and was firmly tied to the tube; anesthesia was continued through the natural airways and the polyethylene tube was closed with gauze or left open according to the type of experiment to be performed.

This method was used in 18 dogs and in 8 the tube was left open so that the animals breathed both through the natural airways and through the polyethylene tube; all these animals died spontaneously and the gross, histologic, and bacteriologic findings were similar to those described in the previous group. In the remaining 10 dogs, the polyethylene tube, communicating with the trachea, was intermittently opened every day for longer periods with the hope of "conditioning" the animals to breathing through the artificial airway. Dog 32 was reoperated upon 18 days later and the cervical trachea was closed so that the only airway was the polyethylene tube; this animal died 6 days later with the same bronchopneumonic picture. On the other hand, in Dog 33, in which the polyethylene tube was closed most of the time, at the time of sacrifice 60 days after the operation, there were no infectious complications; Dog 38, sacrificed 12 days after the operation and in which the tube was also closed most of the time also showed no infection. In Dog 45, the tube was accidentally removed 8 days after operation but the wound healed satisfactorily and the dog was alive and healthy at the time of last observation (30 days). In the last 4 dogs just described, bronchoscopy was performed which revealed the correct position of the tube and the healing of the wound in Dog 45.

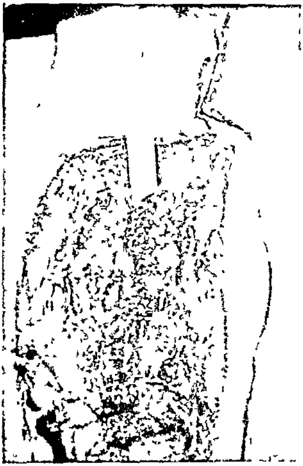

Fig. 3 —The polyethylene tube inside the trachea at the point of emergence from the thoracotomy, the muscular layers are sutured

Pathologic examination of the tissues of 7 animals of this group showed that the polyethylene tube was lying in a duct formed by connective tissue with slight inflammatory reaction, and that, near the trachea, the duct was lined by epidermoid epithelium arising through metaplasia from the tracheal epithelium (Fig. 4).

Group 3.—Partial Endothoracic Tracheostomy With a Polyethylene Tube Covered by Skin.—

In 5 dogs, a portion of skin and superficial muscle, measuring 10 by 6 cm., was removed (Fig. 5) and used as a tube around the polyethylene tube; the skin was sutured around the tracheal opening and again to the margins of the thoracic wound. The polyethylene tube inside the skin tunnel served to avoid collapse (Fig. 6). The animals survived from 1 day to 3 days and the autopsy performed in 4 of them showed infection and separation of the sutures of the skin tunnel to the trachea which adequately explains the presence of empyema and the death of the animals.

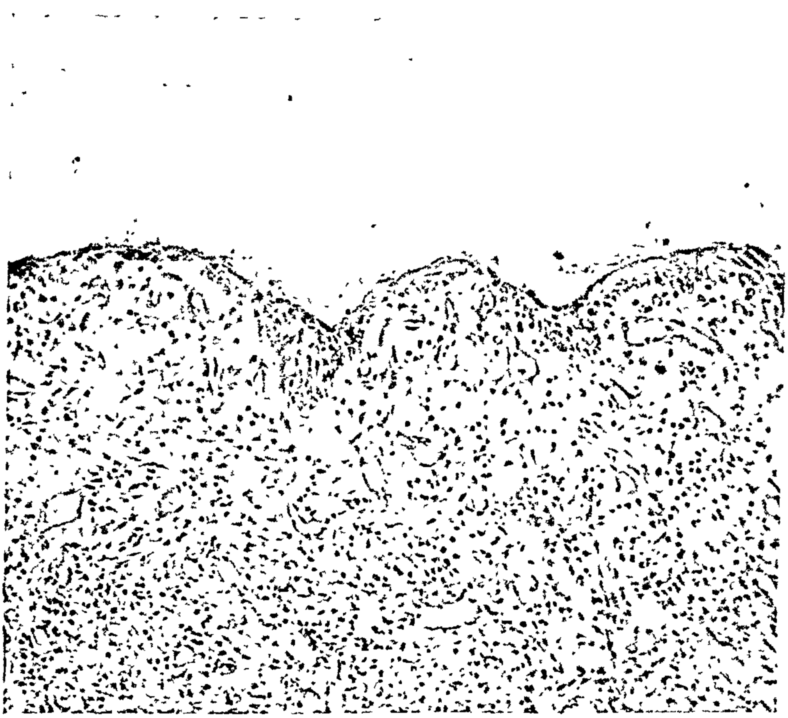

Fig. 4.—Epidermoid metaplasia of the tracheal epithelium near the opening of the tunnel.

DISCUSSION

The surgical technique of experimental transthoracic tracheotomy is relatively simple but care must be observed to leave the new airway as straight as possible in order to avoid accumulation of secretions; the significance of this fact is borne out by the results in the three groups of animals. The anesthesia is also simple and, when complete tracheostomy is performed, it can be continued through the lower segment of the trachea; when tracheostomy is partial, the administration of the anesthetic is better obtained through the natural airway At the end of the operation the animal is breathing normally and no râles can be heard

The animals in the first group died spontaneously with bronchopneumonia in spite of the use of continuous aspiration of the tracheal opening in the chest

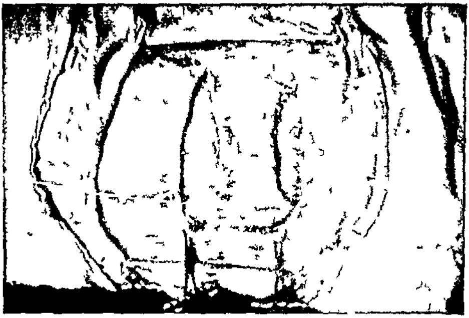

Fig 5—Preparation of the skin graft in the chest of the dog

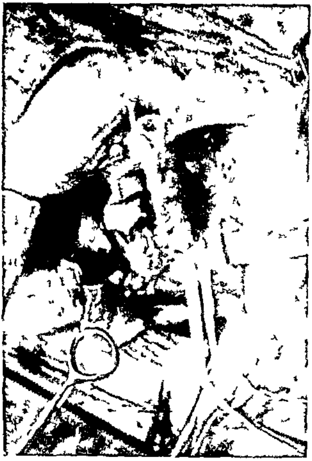

Fig 6—Partial tracheostomy Notice the pedicle skin graft anastomosed to the trachea and sutured as a tunnel containing the polyethylene tube

and the administration of systemic and local antibiotics These results illustrate the significant role played by the upper respiratory tract as a defense mechanism against infections, operated by means of secretions, ciliary activity, temperature, humidity, and the cough reflex suppressed in these animals by anesthesia and specially by the absence of the larynx in the artificial airway. The bacteria isolated from the nasopharynx in 10 healthy dogs were the same as those usually encountered in the lungs and trachea of the animals operated upon (alpha *Str. hemolyticus, M. pyogenes* var. *albus* [nonhemolytic], *Proteus sp., M. pyogenes* var. *aureus,* and *K. pneumoniae*). The immediate postoperative bronchial washings failed to reveal any bacteria in smears or cultures, thus indicating that the lower respiratory tract is normally aseptic.

In Group 2, a polyethylene tube was used to establish communication between the endothoracic trachea and the environment, and in 8 dogs it was left open so that the animals breathed through both the normal and the artificial airways. Since the fate of these dogs was the same as Group 1 it was decided to close the polyethylene tube in the remaining 7 and this changed the outcome immediately since the animals continued breathing through the normal airways. Additional confirmation of the deleterious influence of a bypass of the upper respiratory tract was obtained in Dog 32, which died with bronchopneumonia when the cervical trachea was closed and it could only breathe through the transthoracic tube.

In a series of animals of Group 2, which died 8 or more days after the surgical procedure (Dogs 32, 33, 37, 38, 41, and 45), it was found that the polyethylene tube was surrounded by a tunnel of connective tissue; in the last animal (Dog 45) the tube was accidentally eliminated and the tunnel closed spontaneously together with the tracheal wound. Bronchoscopy in this dog revealed a healed wound in the trachea. It was then thought that the connective tissue tunnel should be replaced by a pedicle skin autograft in order to ensure its permanent patency and 5 animals were operated upon using the polyethylene tube in order to avoid collapse of the skin tunnel. Unfortunately, the sutures of the skin graft to the trachea were defective and the animals died with empyema without allowing adequate time for observation.

We believe that the present work can be continued by placing the animals in a warm and humid atmosphere, which was not feasible at the time it was carried out, and by placing a wire network around the skin in order to avoid collapse of the tunnel, following Gebauer's method[13]; finally, progressive "conditioning" of the animals to breathing through the artifical airway may improve the results obtained in the present series.

SUMMARY

The observation of a group of patients with obstruction of the endothoracic portion of the trachea in which classical tracheotomy was of no avail suggested an experimental study of transthoracic tracheostomy. Forty-six dogs were operated on according to the three following techniques: Group 1, complete transthoracic tracheostomy; Group 2, partial transthoracic tracheostomy with a polyethylene tube; Group 3, transthoracic tracheostomy with a polyethylene tube covered by skin. The results of these studies and of the pathologic and bacteriologic observations in 32 autopsied animals of the series suggest the following conclusions.

1 Complete or partial, transthoracic experimental tracheostomy is a relatively simple procedure

2 Results could be improved by replacing the decontaminating functions of the upper respiratory tract which are lost with the procedure

3 Replacement of such decontaminating functions include an appropriate temperature and humidity of the atmosphere, repeated aspirations instead of the cough reflex, and protection by means of local and systemic antibiotics

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A TECHNIQUE FOR BICUSPIDIZATION OF THE AORTIC VALVE

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Although there are a dozen or more etiologies for aortic insufficiency, the ultimate problem is similar in most cases. There is a disparity between the area of the aortic orifice and the area of valve leaflet with which this orifice must be covered during diastole. Recently, efforts have been made under direct vision to establish a more favorable orifice/valve leaflet ratio by excision of the noncoronary cusp and conversion of the valve to a bicuspid structure.[1-4, 6, 7] Early results by Bailey with the clinical application of this method appear to warrant a more extensive clinical trial.[1, 2]

Concerning the physiologic consequence of this procedure, several problems remained unsettled. Since bicuspidization of the valve reduces the orifice by more than 50 per cent, the effect of the relative stenosis on the left ventricle is of interest. It is also important to know if it is necessary to excise the leaflet of the noncoronary cusp or if this leaflet can simply be defunctionalized. The present investigation is concerned with these questions and with a description of a simplified method for bicuspidization of the aortic valve.

METHODS

Eleven mongrel dogs (8 to 15 Kg.) were used. The operative procedure and all subsequent tests were performed under sodium pentobarbital anesthesia (25 to 30 mg. per kilogram). Surgery was done under hypothermia (27° to 32° C.), cooling and rewarming being done by immersion in water baths of appropriate temperature. Simultaneous pressures were obtained postoperatively by transcarotid catheters and left ventricular puncture, respectively, and were recorded with an inductance manometer which had a frequency response in excess of 30 cycles per second. Heart sounds and electrocardiogram were recorded with a commercial phonocardiogram.

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DESCRIPTION OF OPERATIVE PROCEDURE

Thoracotomy is performed through the right fourth intercostal space. The azygos vein is ligated and the superior and inferior venae cavae encircled with tapes. The pericardium is opened and a stay suture in the auricular appendage is used to retract the right atrium inferiorly (Fig. 1). The cleavage plane between the right atrium and the noncoronary sinus of Valsalva is developed. Finally, the origin of the right coronary artery is identified (Fig. 1). Both venae cavae are then occluded with Rumel Belmont tourniquets and the ascending aorta cross clamped. A longitudinal ascending aortotomy is made and extended proximally through the annulus to the base of the noncoronary cusp (Figs. 1 and 2).

When the lips of the aortotomy are spread and residual blood sucked away a splendid view of the valve is afforded (Fig. 2). The two points of insertion of the noncoronary leaflet are identified. A needle, swedged with 5-0 silk, is placed through these two points, passing from outside in on one side and inside out on the other side (Fig. 2). Having selected these two points for approximation (Fig. 2), an ellipse of excess aortic and annulus tissue is trimmed away on each side down to within 1 mm. of the previously placed suture (Fig. 3, *B*).

The suture is tied, closing a central point of the aortotomy (Fig. 3, *C*). The aortotomy is closed with a continuous suture, starting proximally and oversewing the guide stitch in the middle (Fig. 3, *D*). Before the last sutures are placed, the venae cavae are released to allow air in the left ventricle to be flushed out, and the aortic clamp is removed.

The period of caval occlusion in this series ranged from 7 to 11 minutes. Ten of the eleven dogs developed ventricular fibrillation, with successful resuscitation in all. In several instances, it was necessary to raise the heart temperature by lavaging the chest with warm saline solution before a good beat could be re-established. Blood transfusions were not given.

RESULTS

Operative Mortality and Morbidity.—There was no mortality at the operating table. One dog died of heart failure (with acute pulmonary edema) 6 days after surgery. The 9 remaining dogs lived for chronic study and their behavior and activity were entirely normal.

Ascultatory Findings.—All chronic dogs were examined for heart murmurs at intervals postoperatively and at least one phonocardiographic recording obtained before they were sacrificed. The findings were similar in every case. There was a diamond shaped systolic murmur which was heard most distinctly just to the left of the sternum in the second or third interspace (Fig. 4, *B*). In the same location, the second heart sound was invariably accentuated with a snapping tambour quality (Fig. 4, *B*). In no instance was a diastolic murmur present.

Left Ventricular and Aortic Arch Pressures.—The animals were lightly anesthetized with sodium pentobarbital before they were sacrificed, and

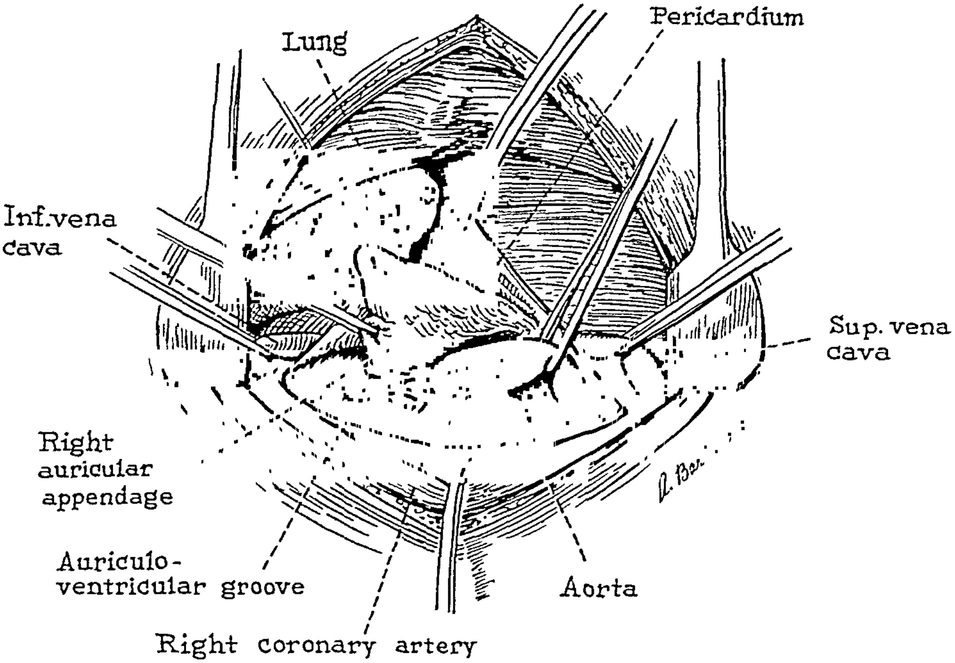


Fig. 1.—View of operative field through right thoracotomy.

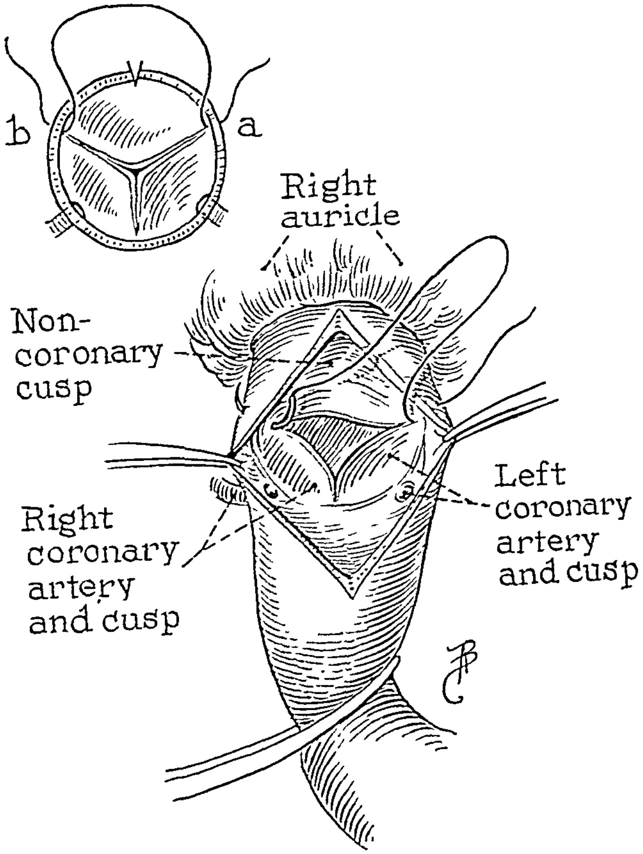


Fig. 2.—Suture at insertions of noncoronary leaflet.

simultaneous pressures obtained from the aortic arch (by retrograde catheterization) and left ventricle (by direct puncture). In no case was a gradient demonstrated between the ventricle and the arch (Fig. 4, *A*). In every case, the aortic pressure complex included a sharp dichrotic notch (Fig. 4, *A*), strengthening the belief that significant regurgitation had not been produced.

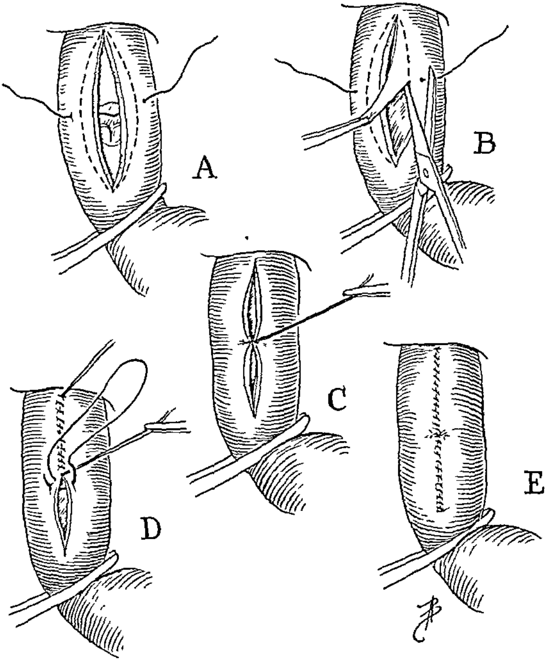
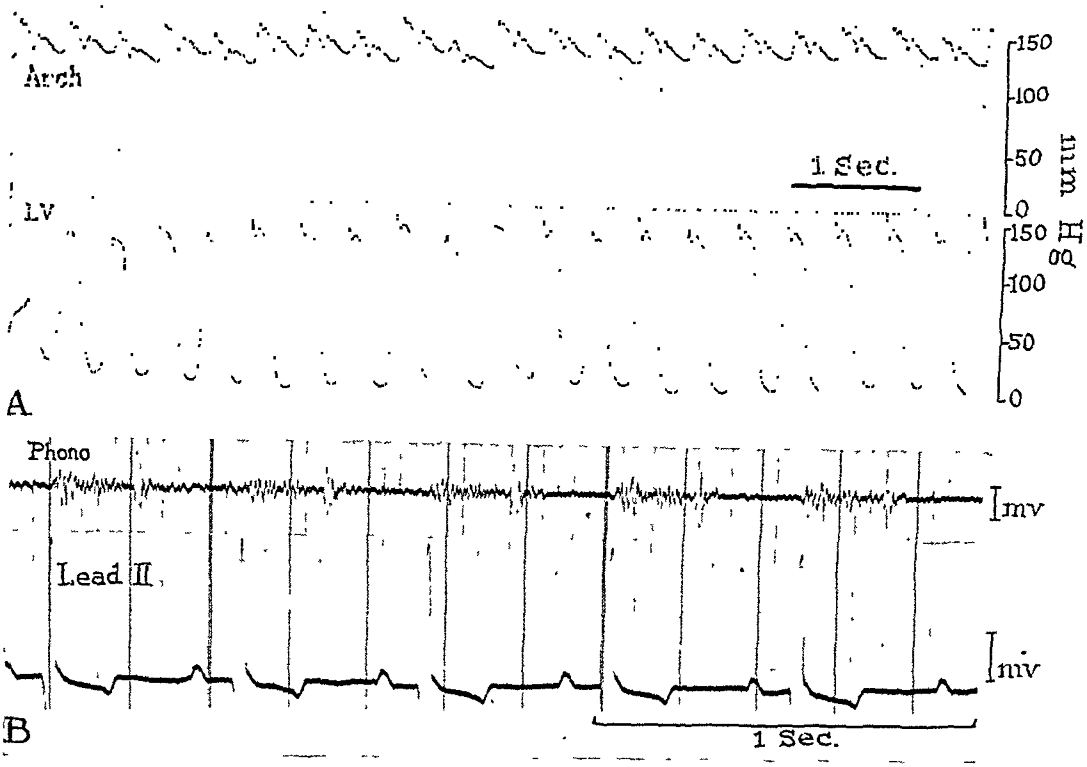


Fig 3.—Excision of excess aorta, annulus, and cusp. Closure of aortotomy.

Effect of the Operative Procedure on Left Ventricular Weight.—Before sacrificing the animals, accurate body weights were obtained. At autopsy, dissection on the left ventricle was performed by the method of Goodale and Hackel[8] and the dissected left ventricle weighed. The actual weight of the left ventricle was compared with the left ventricular weight which was anticipated on the basis of body weight according to the Goodale-Hackel coefficient. As a control, hearts from 18 dogs sacrificed in various acute experiments were also weighed (Fig. 5).

The left ventricular weights of the normal control dogs are seen on the left in Fig. 5. On the right, expressed in per cent of predicted weight, are depicted the left ventricular weights of the 9 chronic dogs at various times after aortic

A.



B.

Fig. 4.—Pressures, phonocardiogram, and electrocardiogram 3 months postoperatively (Dog 9).

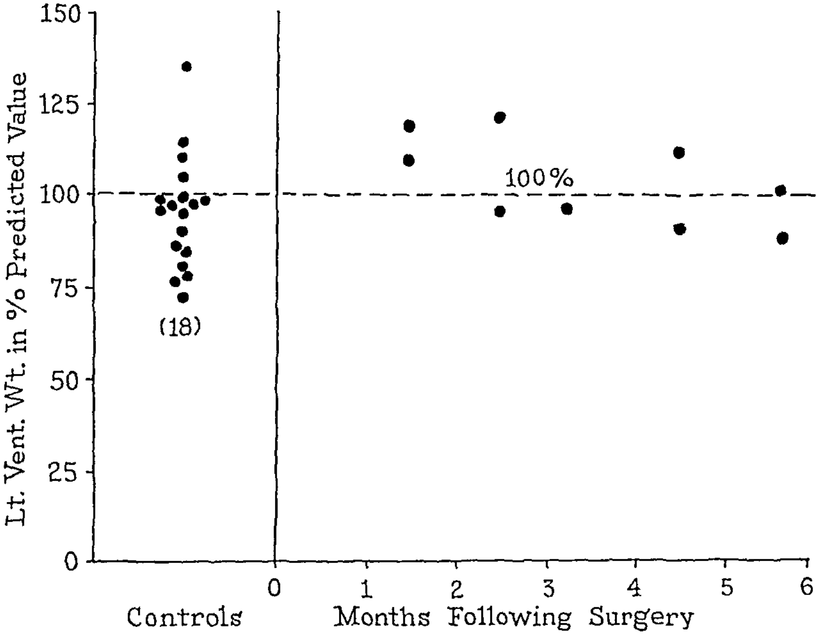


Fig. 5.—Left ventricular weights at autopsy, expressed as per cent predicted value. Control dogs are at left.

valve bicuspidization. It is seen that in 4 cases the weights were slightly less than predicted, in 4 cases slightly greater, and in one case exactly the same. Thus, in the series studied, there is no evidence of hypertrophy up to 6 months postoperatively.

Autopsy Findings.—Two animals died 6 days postoperatively, one as a result of empyema and the other of heart failure. Nine animals were electively sacrificed at 6 weeks to 5½ months postoperatively. The reconstructed valves were examined with care and sections of liver and lung taken for histologic study

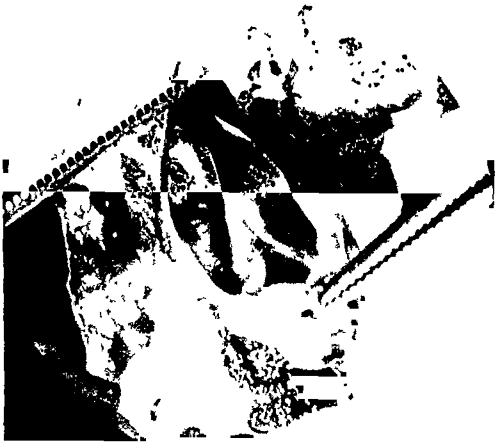


Fig 6 —Aortic valve in dog (Case 10) in which spread of aortotomy suture line had allowed valve to resume partially tricuspid structure

In all dogs except one (Case 10), the valves had remained bicuspid. The prolapsed noncoronary cusp was found to be delicate and to be the seat of vegetations in no case In Case 10, the suture line had spread approximately 2 mm (Fig. 6). It is interesting that pressures from this animal were entirely normal and that there was no evidence of a diastolic murmur on the phonocardiogram, suggesting that the noncoronary cusp had resumed function and prevented the development of aortic insufficiency.

Excepting the dog which died of pulmonary edema in the immediate postoperative period, there was no gross evidence of heart failure in any animal One of the 9 animals studied chronically had histologic evidence of chronic passive congestion of the liver and lungs (Table I).

TABLE I

NO.	WEIGHT (KG.)	DURATION	L. VENTRICULAR AORTIC GRADIENT	SYSTOLIC MURMUR	DIASTOLIC MURMUR	AUTOPSY FINDINGS
1	12.7	11 wk.	0	+	0	Valve bicuspid; no gross failure; chronic passive congestion histologically
2	9.0	6 da.				Died of empyema; valve bicuspid
3	9.1	18 wk.	0	+	0	Valve bicuspid; no gross or microscopic evidence of failure
4	10.0	20 wk.	0	+	0	Valve bicuspid; no gross or microscopic evidence of failure
5	9.0	17 wk.	0	+	0	Valve bicuspid; no gross or microscopic evidence of failure
6	10.0	6 da.				Valve bicuspid; gross and histologic pulmonary edema
7	11.0	22 wk.	0	+	0	Valve bicuspid; no gross or microscopic evidence of failure
8	13.2	7 wk.	0	+	0	Valve bicuspid; no gross or histologic evidence of failure
9	15.9	10 wk.	0	+	0	Valve bicuspid; no gross or histologic evidence of failure
10	8.6	6 wk.	0	+	0	Valve had 2 mm. separation suture line and defunctionalized valve covered gap; no gross or histologic evidence of failure
11	10.4	22 wk.	0	+	0	Valve bicuspid; no gross or microscopic evidence of failure

DISCUSSION

The fundamental geometric alteration produced by aortic valve bicuspidization is shown in Fig. 7. The effect on the orifice area of removing one third the circumference is expressed by the formula

$$\frac{Ax}{Ay} = \left(\frac{Cx}{Cy}\right)^2 \text{ or } Ay = \tfrac{4}{9} \text{ the original area}$$

in which Ax = original orifice area = 1; Ay = reconstructed orifice area; Cx = original circumference = 1; and Cy = reconstructed circumference = $\frac{2}{3}$.

Since the leaflet area which is defunctionalized or removed is one third (one leaflet), the end ratio of $\frac{\text{new leaflet area}}{\text{new orifice area}}$ is $\frac{2/3}{4/9}$ or 1.49. Although the calculations indicate that the bicuspid valve now has 1.49 more leaflet area than orifice area, it is possible that deformation of the leaflet attachments reduces this ratio. It is quite clear, however, from examination of the gross valve, that the bicuspid valve has more leaflet than is necessary to cover the reconstructed orifice. It is probably the excess of leaflet tissue that accounts for the accentuated and tambour second heart sound after surgery.

Previous studies on aortic valve bicuspidization[6] have emphasized removal of the noncoronary leaflet as an integral part of valvuloplasty because of the fear that the prolapsed leaflet would cause aortic insufficiency. The present study suggests that excision of the leaflet is not uniformly necessary. Aortic insufficiency did not develop in any case in the present study. In fact, in one of the dogs (Case 10) some spreading of the aortotomy suture line occurred, leaving a gap at one end of the remaining two leaflets. This gap was covered by the prolapsed leaflet which had apparently resumed function.

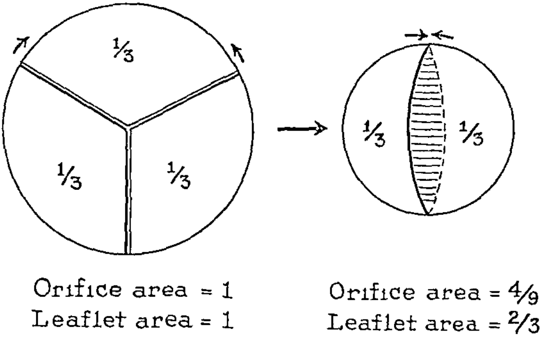


Fig 7.—Geometric changes after bicuspidization

The issue of whether or not the leaflet must invariably be removed would appear to be of more than academic interest in assessing the potential value of the described procedure in the treatment of clinical aortic insufficiency. In patients with regurgitation, the disparity between available leaflet and the orifice area seldom exceeds 25 per cent and is usually less. Restoration of valve competence would often not require such radical rearrangement of valve structure as with total bicuspidization. Rather, it would seem that treatment could consist of excision of a *portion* of the noncoronary annulus with retention of the tricuspid valve as suggested by Hufnagel.[9] Improvement in the $\frac{\text{leaflet area}}{\text{orifice area}}$ ratio would occur according to the amount of annular circumference excised and the reduction in orifice area could again be calculated from the formula $\frac{A_x}{A_y} = \left(\frac{C_x}{C_y}\right)^2$ as outlined above.

The operative procedure described would afford considerable versatility in the treatment of aortic insufficiency. According to the particular needs of the case, one could excise a portion of the noncoronary annulus, excise the entire noncoronary annulus with defunctionalization of the valve, or excise both the annulus and leaflet. In the last case, excision of the leaflet can be done with the addition of only a few seconds to the operating time.

The operative procedure in the present study was done with inflow occlusion and hypothermia, necessitating haste and the routine use of resuscitative measures. Undoubtedly, a more desirable approach in clinical application would be the use of extracorporeal circulation with coronary perfusion.

SUMMARY

1. A simplified method is described for conversion of the aortic valve from a tricuspid to a bicuspid structure. Under conditions of hypothermia and inflow occlusion, the operative mortality is 10 per cent.

2. The noncoronary cusp can be completely or partially removed with this technique and the valve leaflet either defunctionalized (as was done in this series) or removed.

3. In dogs studied chronically, there was no evidence of physiologically significant aortic stenosis or aortic insufficiency. Left ventricular weights up to 5½ months postoperatively were within normal limits.

4. The geometric alterations produced in the aortic valve after bicuspidization are subjected to analysis. The applicability of this technique in the treatment of clinical aortic insufficiency is discussed.

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ARTERIOVENOUS FISTULA BETWEEN THE INTERNAL MAMMARY ARTERY AND VEIN FOLLOWING STAB WOUND OF THE CHEST

A Case Report

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PENETRATING wounds of the anterior wall frequently cause injury to the internal mammary and intercostal vessels since the ribs afford very little protection to these structures Laceration of these vessels is followed by intrathoracic or extrathoracic bleeding While penetrating injuries to other peripheral vessels may result in arteriovenous fistula or aneurysm, a review of the literature fails to reveal a report of an arteriovenous communication developing in the internal mammary vessels following trauma Elkin and Warren,[1] in reviewing experience in 400 patients having arteriovenous fistulas incurred during World War II, encountered one communication between the internal mammary artery and innominate vein Seeley and Elkin[2] have reviewed 106 instances of either arteriovenous fistula or false aneurysm occurring in 101 patients injured in the Korean War Over 90 per cent of these occurred in the upper or lower extremities, with arteriovenous fistula occurring twice as frequently as false aneurysm

Glenn and Steinberg[3] have reviewed the literature on arteriovenous fistula occurring incident to mass ligation of vessels following surgical procedures and report a case of arteriovenous fistula of the internal mammary artery occurring 2 years after radical mastectomy

Arteriovenous fistulas may also be congenital in origin, but trauma is a much more common cause A single case of congenital arteriovenous fistula of the internal mammary vessels has been reported by Wells and Hurt [4]

The following case illustrates the occurrence of an arteriovenous fistula between the internal mammary artery and vein following a stab wound of the chest

CASE REPORT

A 25 year old Negro woman was admitted to Kansas University Medical Center on Jan 28, 1958, with a history of having been stabbed in the right anterior chest 43 days previously by an assailant wielding a kitchen knife She had received emergency treatment

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*This work was done in whole under an American Cancer Society Clinical Fellowship held by Dr Brownlee present address 1616 North Norton Medical Square Tucson Ariz

**Present address 920 West 47th Street Kansas City 1- Mo which included primary closure of the wound with sutures. Within a few hours, a painful swelling at the site of injury had developed for which an injection of an analgesic was given to relieve the pain.

A week later the skin sutures were removed. The pain and swelling still persisted and, 2 weeks following her injury, a physician incised the wound, thinking an abscess was present. Instead a jet of blood was released which sprayed the office wall. The bleeding was controlled with considerable difficulty by a combination of sutures and pressure bandages. Sufficient bleeding had occurred to make her noticeably weak for a few days.

Five days prior to admission she had consulted another physician who incised the mass and expressed several blood clots. Examination, upon admission to Kansas University Medical Center, revealed a nontender, fixed, pulsatile mass overlying the right parasternal region from the second to the fourth intercostal spaces. The mass measured 7 by 3.5 cm. and projected 1.5 cm. beyond the surrounding skin. On the apex there was a crust at the site of the original stab wound and subsequent incisions (*Fig.* 1). A distinct bruit was heard over the mass.

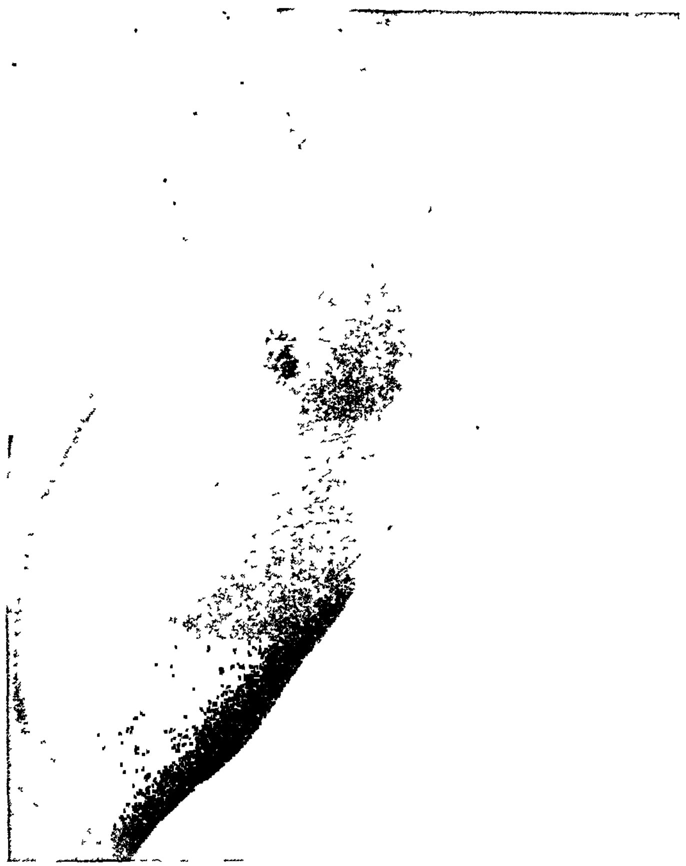

Fig. 1.—External surface of arteriovenous fistula between right internal mammary artery and veins shown by tangential view of the right parasternal area.

The blood pressure was 140/70 mm. Hg; pulse 80; temperature 98.6° F.; hemoglobin 11.0 Gm.; white blood count 4,950; VDRL nonreactive. Chest roentgenograms *did not disclose the mass and showed a normal* cardiac silhouette.

On Feb. 1, 1958, a right parasternal elliptical incision was made around the mass. The internal mammary vessels were exposed over the second and fourth intercostal spaces without entering the thorax. The internal mammary vessels were enlarged and there was visible pulsation of the internal mammary vein proximally and distally to the mass. The internal mammary vessels were isolated and each was ligated in continuity in the second and in the fourth intercostal spaces to prevent subsequent hemorrhage. The mass was dissected free and was found to have a pedicle, consisting of an artery arising from the internal mammary artery and venous channels joining the internal mammary vein (Fig 2). The vessels in the pedicle were individually ligated and divided and the wound was closed in layers

The specimen consisted of an endothelial lined cystic structure containing blood clots and an organizing thrombus There were no postoperative complications.

COMMENT

In this case there was a penetrating injury of the anterior thorax, with laceration of the internal mammary vessels. An arteriovenous fistula resulted and this fistula was associated with a sac formed by the wall of the organizing hematoma. There was a continuous murmur, intensified during systole, and a pulsatile mass present. There were no systemic circulatory manifestations present in this case. The dissected specimen, showing the three distinct venous channels and a single arterial vessel communicating with a common sac, confirmed the presence of an arteriovenous fistula. Surgical excision of the arteriovenous fistula with ligation of the involved vessels was curative.

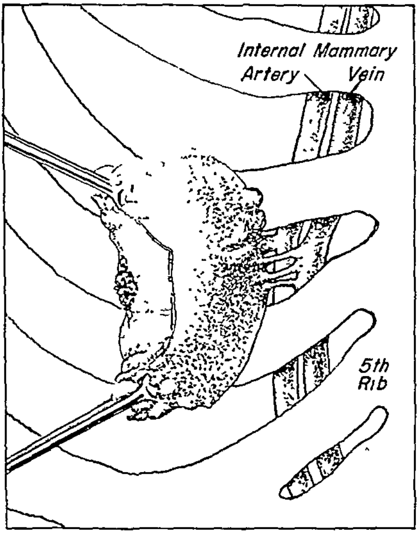

Fig 2—Diagram of arteriovenous fistula between right internal mammary artery and vein

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ASPHYXIATION DUE TO SIMULTANEOUS RUPTURE OF BRONCHUS AND PULMONARY ARTERY

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A NUMBER of accident victims are dead on arrival at hospitals, and an additional number die during attempts at resuscitation. In the following 2 patients, the cause of death was asphyxiation due to bleeding from a torn pulmonary artery into a torn bronchus. These cases are reported in explanation of some of these deaths and in the hope that, if this probability is borne in mind, an occasional patient may be saved.

CASE REPORTS

CASE 1.—F. W., a 9-year-old Negro girl, was admitted to the emergency room at Parkland Hospital (Dallas, Texas) shortly after 7:00 A.M. on Sept. 2, 1951. The child had been shot with a 32 caliber revolver accidentally and had either coughed or vomited a small amount of blood following the injury.

On examination, the child was semi-stuporous and pulse and blood pressure were unobtainable. A wound of entry was located in the right sixth intercostal space under the breast, and roentgenograms revealed a fracture and some metal fragments on the eighth right posterior rib and a hemopneumothorax. The bullet was lodged in the subcutaneous tissues at the level of the fourth posterior rib in the right posterior axillary line.

Initial treatment consisted of closed drainage of the right pleural space, and administration of 500 c.c. of lactate Ringer's solution and 1,000 c.c. of blood. The blood pressure rose to 90/60 mm. Hg, and 1,000 c.c. of blood drained into the bottle, as well as much air. A hemoglobin determination after resuscitation was reported as 14.2 Gm. per 100 c.c. of blood. The child's pulse, blood pressure, and general condition remained stable.

Because of the location of the wound, a diaphragmatic injury and, perhaps, a liver injury were suspected. A right thoracotomy and possible thoraco-abdominal exploration were recommended. In the operating room, induction of general anesthesia was accomplished without difficulty using cyclopropane and ether. As soon as the endotracheal tube was put in place, a gush of blood flowed out. The airway was suctioned, the right chest was opened rapidly and the hilum of the right lower lobe was first clamped with finger pressure and then with a noncrushing vascular clamp. This took approximately 2 minutes from the time of intubation. However, the heart was in total standstill, and massage and other measures failed to reinstate cardiac contractions.

At postmortem examination, the diaphragm was not perforated but there was an area where the bullet grazed the diaphragm. Immediately beneath this there was a subcapsular contusion of the dome of the liver with a slight tear in the capsule.

The right lung weighed 240 grams and there was evidence of fresh and old blood in the bronchi. A hole, measuring 4 mm. in diameter, was found on the inferior surface of the right lower lobe. The lobe was distended and firm. The lower portion of the middle lobe appeared similar. There were blood clots and some fresh blood seen throughout the

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bronchi on the right side The bullet had apparently traversed a segmental bronchus to one of the basal segments of the right lower lobe and had also made a hole in the adjacent segmental pulmonary artery.

The left lung weighed 150 grams, contained a moderate amount of blood in the bronchi, and a large amount of frothy bloody material with a few clots

CASE 2—S H, a 6 year old white girl, was admitted to the emergency room at St Paul Hospital (Dallas, Texas) a little after 1 00 P M on Dec 29, 1958 The child had been struck by a vehicle while crossing the street She reached the emergency room approximately 45 minutes after the accident

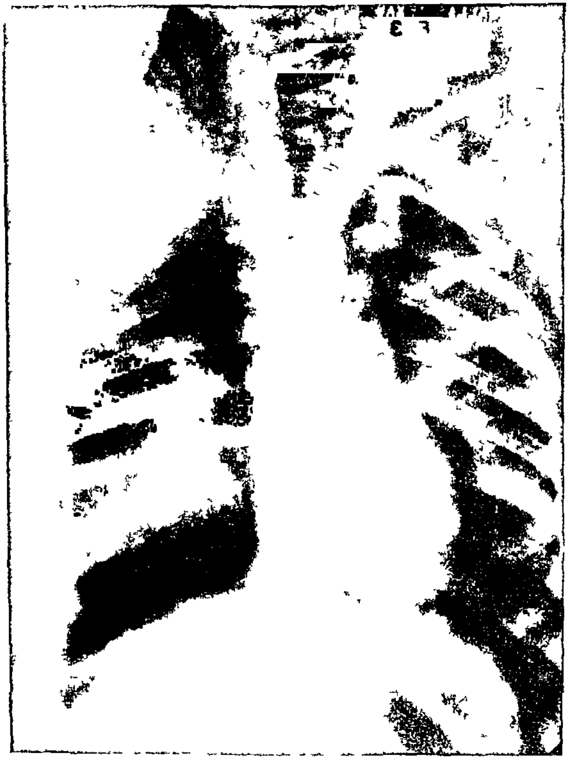

Fig 1—Roentgenogram taken with a horizontal beam the patient lying on the right side shows right tension pneumothorax mediastinal shift, and mediastinal and cervical emphysema

Initial examination revealed an abrasion of the left temple, a comatose, nonresponsive child with no perceptible pulse or blood pressure, with the following salient points noted in the physical examination: The pupils were dilated, reacted to light, and appeared equal There was moderate subfascial cervical emphysema bilaterally and moderate subfascial pectoral emphysema on the right. The breath sounds were absent over the right chest,

BOW MATTRESS SUTURE FOR CHEST CATHETERS

James Bernard Seaman, M.D., Tyler, Texas*

WE PROPOSE a method of prevention of air and fluid leakage about a chest catheter in place, and through the tube wound after the catheter has been withdrawn.

No one can deny that lack of control of the situation can add to pleural space problems such as pneumothorax and empyema, especially when negative pleural space pressure may be inordinately high, and add to loss of fluid into a dressing with invitation to infection.

Since 1947 we have seen many methods of control used. The present technique has been employed for many months and has been adopted as a standard part of our regimen.

It consists essentially of a horizontal mattress suture of 0 cotton (Fig. 1) through the skin and subcutaneous tissues with the loop or bight around the catheter and with the suture ends normally located cephalad to facilitate later extraction of the catheter by an assistant, and tying of the knot by the operator. This suture may be applied either before or after the catheter is placed in position in the chest wall.

With the catheter in place, a friction knot (first knot or double overhand of a surgeon's knot) is then tied. A double bow knot is then tied securely with the suture ends longer than the bows. This serves then as a purse string suture through the soft tissues, about the catheter, which effectively seals against movement of air or fluid.

A small clamp of the mosquito type is then placed across the bows and suture ends until the time of securing the wound dressing. The clamp is lifted to make the suture taut alongside the catheter and narrow adhesive tape is placed around the catheter in spiral fashion securing the suture material to the catheter. The catheter is thus doubly secured and tugging on the catheter or connecting hose serves only to tighten the soft tissues about the catheter. Being prudent, we attain additional protection with tape over the skin, onto the dressing, and onto the catheter.

In removing the catheter one simply grasps the suture (bows and ends), unwinds the spiral tape, unties the bow as when untying shoe strings, and

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From the Department of Surgery, East Texas Tuberculosis Hospital, Tyler, Texas.
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loosens the friction knot if necessary with a clamp. An assistant extracts the catheter on command, and the operator promptly pulls the friction knot tight and completes a surgeon's knot.

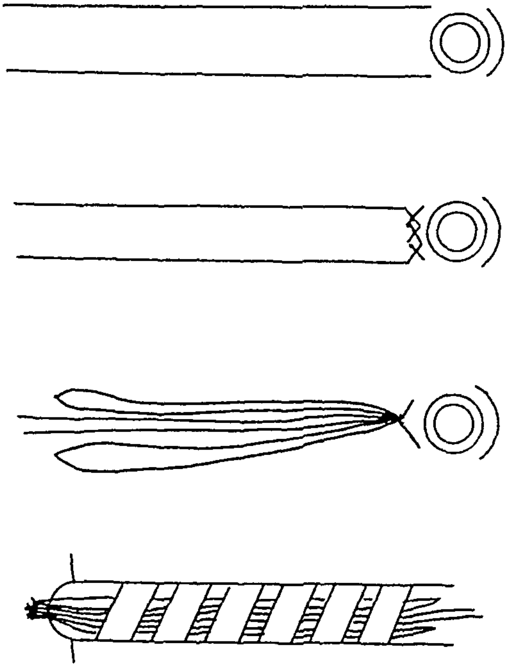

Fig. 1.

We have experimented with many methods and are of the opinion this is the best. It may be original with us. There has been no fluid or air exchange about the catheter, no tissue necrosis, and no early or late abscess of the chest wall. If no assistant is available the routine may be followed successfully by one individual. There is one precaution—if one is forced to use a soft catheter one must be careful not to obstruct the lumen when tying the friction knot.

Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Fortieth Annual Meeting of The American Association for Thoracic Surgery will be held May 11, 12, and 13, 1960, in Miami Beach, Florida Headquarters will be the Deauville Hotel

Requests for Hotel Reservations

These should be mailed directly to Mrs Mildred Sander, Reservation Manager, Deauville Hotel, Miami Beach, Florida Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure If accommodations are desired elsewhere please communicate directly with the hotel of your choice

Material for the Program

Scientific Papers—Abstracts of all papers proposed for presentation at the 1960 meeting *must be received on or before* **November 15, 1959,** otherwise they will not be considered by the Program Committee These should be labeled "For Thoracic Surgery Forum" or "For Regular Program" depending upon the nature of the subject matter, in the same manner as in previous years They should contain from 200 to 250 words that accurately reflect the content of the completed paper

Six, repeat, six clearly legible copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, 308 Carondelet Building, 7730 Carondelet Avenue, St Louis 5, Missouri

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary *immediately* after their presentation If they are not ready at that time there is a chance that they will not be published in The Journal of Thoracic and Cardiovascular Surgery

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than* **November 15, 1959,** otherwise the application will be deferred for consideration until the 1961 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Frank Gerbode, M.D.
Chairman of the Membership Committee
Stanford University Hospital
San Francisco 15, California

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applicants be held over for reconsideration a *second year.*

The Journal of
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NUMBER 3

Original Communications

STUDIES OF PULMONARY DIFFUSION AFTER OPEN HEART SURGERY

Robert J. Schramel, M.D. (by invitation), Robert Cameron, M.D. (by invitation), Morton M. Ziskind, M.D. (by invitation), Maurice Adam, M.D. (by invitation), and Oscar Creech, Jr., M.D., New Orleans, La.*

Since the earliest days of open heart surgery with extracorporeal circulation, there have been reports of severe pulmonary complications developing after operation. While increasing experience has done much to reduce the incidence of these complications, a large proportion of patients still require assisted respiration, tracheostomy, and prolonged oxygen therapy during the postoperative period. It is correct perhaps to assume that any functional alteration in the lungs, resulting from extracorporeal circulation, is due to injury to the pulmonary capillaries or the alveolar membrane and that this is reflected in alterations of pulmonary gas diffusion. This report is concerned with measurements of the carbon monoxide diffusing capacity (D_{CO}) in human beings and in experimental animals before and after cardiopulmonary bypass. The "steady state" diffusing capacity[1] for carbon monoxide is ideally suited to the studies of these patients since it permits some assessment of ventilatory function, as well as the diffusing function of the lung, without requiring any unusual effort on the part of the patient.

From the Departments of Surgery and Medicine, Tulane University, and the Cardiopulmonary Laboratory, Veterans Administration Hospital, New Orleans, La., Charity Hospital of Louisiana, and Touro Infirmary.

Supported in part by the Louisiana Heart Association and U.S. Public Health Service Grant HTS-5170, the Jones County Texas Tuberculosis Association, and the Tuberculosis Association of Greater New Orleans

Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

*Fellow, National Institutes of Health.

METHODS

Carbon monoxide diffusing capacity (D_{CO}) was determined by the method of Filley, MacIntosh, and Wright[1] with a few modifications. To minimize hypoxemia, the subjects inspired a gas mixture of 0.1 per cent CO in 30 per cent O_2 rather than the usual 0.1 per cent CO in air. Carbon dioxide pressure was calculated after determination of the pH, hematocrit, and CO_2 content of arterial blood. Seven adult patients had carbon monoxide diffusion studies done preoperatively and, on several occasions, after open heart surgery. Diagnoses in these patients are listed in Table I. Only 1 patient (No. 6) had any evidence of intrinsic pulmonary disease. This was marked by chronic cough with expectoration associated with excessive smoking. Determinations were additionally performed on 2 patients undergoing thoracotomy without cardiopulmonary bypass.

TABLE I. CLINICAL STUDIES

PATIENT NUMBER	INITIALS	AGE	DIAGNOSIS
1	H. D.	30	Aorta-RA fistula
2	Z. M.	47	Mitral insufficiency
3	J. M.	27	Aorta-RV fistula
4	N. C.	18	Atrial septal defect
5	H. S.	29	Ventricular septal defect
6	A. M.	52	Atrial septal defect
7	J. J.	32	Aortic stenosis
8	Y. F.	32	Mitral stenosis*
9	J. T.	65	Hiatus hernia*

*Not on extracorporeal circulation.

Preoperative and postoperative determinations of diffusing capacity were also performed on 5 mongrel dogs undergoing unilateral thoracotomy of 15 minutes' duration. In another group of 5 dogs, determinations (D_{CO}) were made before and after establishment of extracorporeal circulation without thoracotomy. This was done by inserting No. 18 Fr. polyethylene catheters into the right atrium through the common femoral and external jugular veins. These were connected to the venous line of a DeWall bubble oxygenator. Oxygenated blood was returned to the animal through a femoral artery. Two additional dogs were studied before and after cardiopulmonary bypass established through a right thoracotomy. In these animals, extracorporeal circulation and inflow occlusion were maintained for 15 minutes. In all animal experiments, a cuffed endotracheal tube was inserted. Animals were anesthetized with veterinary Nembutal 15 mg. per kilogram of body weight. Further anesthesia was provided by continuous intravenous administration of Nembutal in dilute solution (6 mg./c.c.) so that the respiratory rate was maintained at 18 to 30 per minute. Ventilation during thoracotomy in animals was maintained by an automatic respirator utilizing room air. The lungs were not inflated during cardiopulmonary bypass in dogs or patients.

A DeWall pump-oxygenator system was used in all animal experiments and in Patients 1 and 3. Oxygenation was obtained by bubbling 100 per cent

O_2 through the blood in this system. In the remaining patients, a Kay Cross rotating disc oxygenator was used. In this system, oxygenation was secured by exposing blood to a mixture of 95 per cent O_2 and 5 per cent CO_2.

All patients subjected to open heart surgery in this study were considered good operative risks. Perfusions in all instances were conducted at maximum flow rates, that is, limited only by the volume of venous return. Satisfactory repair of all defects was accomplished with the exception of Case 2 in whom significant mitral regurgitation persisted after operation. No postoperative pulmonary complications of unusual magnitude appeared except in Case 2. Temporary atelectasis of the left lower lobe occurred in Case 6 and responded to bronchoscopic aspiration.

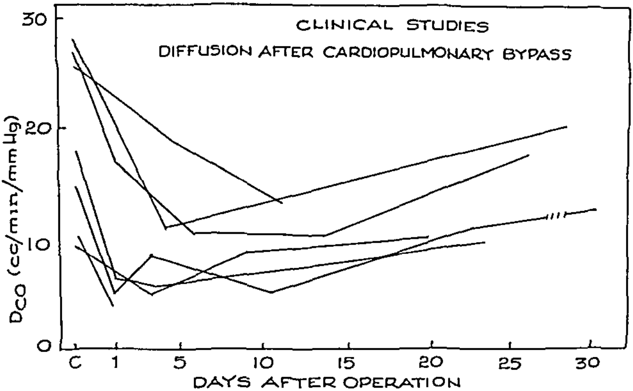

Fig 1—Carbon monoxide diffusing capacity before and after open heart operations. C on the ordinate represents a preoperative determination which may have been done 1 to 7 days before operation.

RESULTS

In each of the 7 patients, undergoing open heart surgery, there was an increase in total ventilation (V_L) after operation, but in no instance did it exceed 15 per cent of the predicted maximum breathing capacity (MBC) for the individual. Tidal volume (V_T) was essentially unchanged or reduced immediately following operation. The physiologic dead space (V_D) was increased in all patients except No 5. In part, this could be accounted for on the basis of an increased frequency of respiration, but it more likely represented an unfavorable alteration of the ventilation perfusion relationship in the immediate postoperative period. For the most part, alveolar ventilation (V_A) was effectively maintained. Two patients (Nos 4 and 6) exhibited small reductions of V_A and there were increases of similar magnitude. Ventilation equivalent (V_O [c c /min] V_L [L /min]) was within normal range, both before and after operation in all cases except No 2 in whom it was slightly abnormal. Oxygen consumption increased somewhat after operation, usually from the fourth to the eleventh day, and then returned to control levels. The *diffusion capacity* for carbon monoxide, however, was uniformly reduced after operation to 25 to 40 per cent of preoperative values (Fig. 1). In 3 cases (Nos. 1, 3, and 4), the lowest values were still within the accepted range of normal for these laboratories. In the remaining 4 patients, depression to definitely abnormal levels was observed. In 4 patients (Nos. 1, 3, 4, and 5), the control values were at the upper limits of normal. All of these patients had left-to-right shunts of considerable magnitude. In only 1 patient (No. 6) with a left-to-right shunt was the D_{CO} reduced below normal prior to operation, and this patient had chronic lung disease.

TABLE II. CLINICAL STUDIES

PATIENT	DAYS	V_L	V_T	V_D	V_A	V_{O_2}	pCO_2	D_{CO}
No. 1	0	4.39	334	69	2.54	156	40	25.7
	4	6.36	338	122	3.24	196	38	19.3
	11	5.80	386	159	3.29	159	34	13.9
No. 2	0	4.22	336	95	2.46	138	44	10.4
	1	6.82	272	103	3.11	142	35	3.8
No. 3	0	2.64	459	90	1.82	115	40	27.6
	1	4.00	317	118	1.46	137	47	17.4
	5	5.49	464	165	3.01	163	40	10.7
	13	5.08	505	132	3.29	164	41	10.5
	26	3.93	546	121	2.73	144	41	17.9
No. 4	0	3.97	506	127	2.90	124	36	28.0
	4	4.01	295	98	2.08	170	46	11.4
	13	4.65	387	152	2.31	147	45	14.5
	27	3.64	364	134	2.10	123	43	19.6
No. 5	0	3.20	280	68	1.90	132	42	18.9
	1	3.37	278	70	1.90	117	41	7.0
	3	3.37	303	78	2.00	129	40	5.9
	24	4.14	333	83	2.50	157	37	10.0
No. 6	0	4.08	377	73	2.78	136	35	10.0
	3	4.91	308	134	2.05	153	43	5.2
	9	4.76	380	132	2.53	146	41	9.2
	21	3.90	457	154	2.01	131	40	10.6
No. 7	0	5.62	546	181	3.26	188	39	15.5
	1	8.73	424	226	3.14	215	39	5.4
	3	7.94	466	223	3.38	236	45	8.5
	10	6.26	520	212	3.17	229	42	5.8
	24	4.96	520	210	2.80	166	40	12.0
	37	5.20	552	212	2.78	140	37	13.8
No. 8	0	4.93	368	99	3.6	174	42.5	12.7
	1	3.77	264	66	3.42	140	43	5.31
	4	4.37	306	68	3.38	176	44	7.22
	11	4.79	278	58	3.8	154	39.5	7.26
	17	4.04	285	66	3.1	152	42	11.7
No. 9	0	3.32	598	176	2.32	149	40	16.3
	1	1.80	275	82	1.27	113	43	7.64
	5	2.87	474	140	2.02	147	39	15.8
	8	3.40	465	141	2.32	153	35	14.6

V_L = Minute ventilation (L./min./M.^{2})
V_T = Tidal volume (c.c.)
V_D = Dead space (c.c.)
V_A = Alveolar ventilation (L./min./M.^{2})
V_{O_2} = Oxygen consumption (c.c./min./M.^{2})
D_{CO} = Diffusing capacity for CO (c.c./min./mm. Hg)

In 4 patients of this series, D_{CO} was measured using 0.1 per cent carbon monoxide in room air. In these 4 patients, the lowest values of D_{CO} were associated with the development of arterial hypoxemia. This hypoxemia was moderate in degree, ranging from 74 to 88 per cent.[2] Values for pH were normal or slightly elevated in those patients who had pronounced increases in alveolar ventilation. The pCO_2 was closely related to the alveolar ventilation which it followed in the expected manner. One patient studied before and after a closed valvulotomy for mitral stenosis showed a pattern of respiratory function after operation similar to that of the patients undergoing open heart surgery, in that the extent and duration of depression of D_{CO} was about the same. Another patient studied before and after transthoracic repair of hiatus hernia developed a marked depression of the D_{CO} on the first postoperative day, which reverted to normal, however, by the fifth postoperative

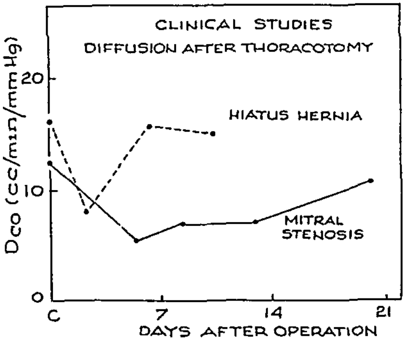

FIG 2.—Carbon monoxide diffusing capacity before and after thoracotomy without cardiopulmonary bypass

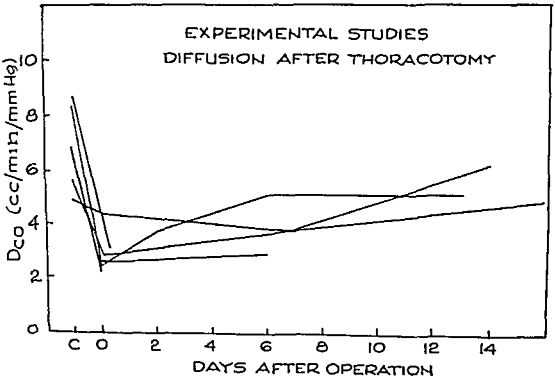

FIG 3.—Carbon monoxide diffusing capacity before and after unilateral thoracotomy in the dog

day (Fig. 2). This patient, unlike the open heart cases, had moderate alveolar hypoventilation after operation.

In 4 of 5 dogs subjected to unilateral thoracotomy, there was a depression of the D_{CO} on the first postoperative day with a gradual return to control levels (Fig. 3). The fifth dog showed essentially no change. In 2 of the 4 animals tested before and after perfusion without thoracotomy, there was essentially no change in the D_{CO} (Fig. 4). In 1 dog, a marked depression of

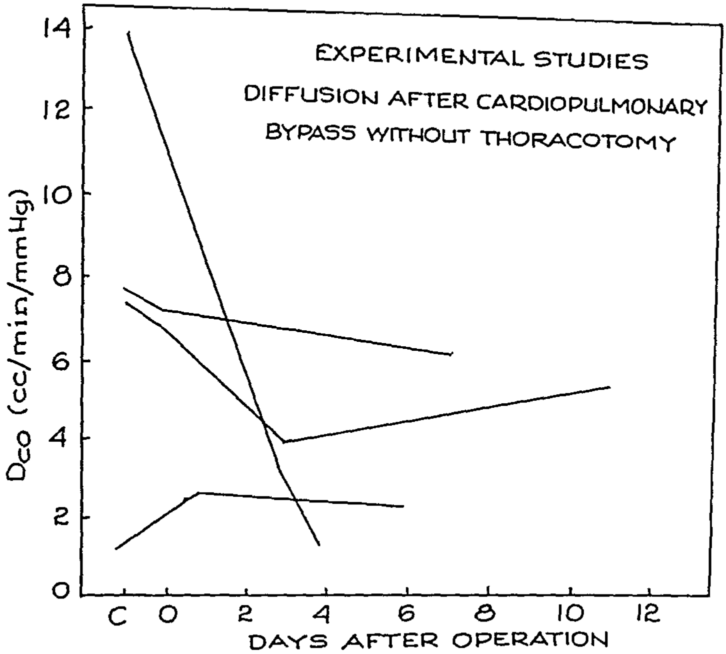

Fig. 4.—Carbon monoxide diffusing capacity before and after perfusion without thoracotomy in the dog.

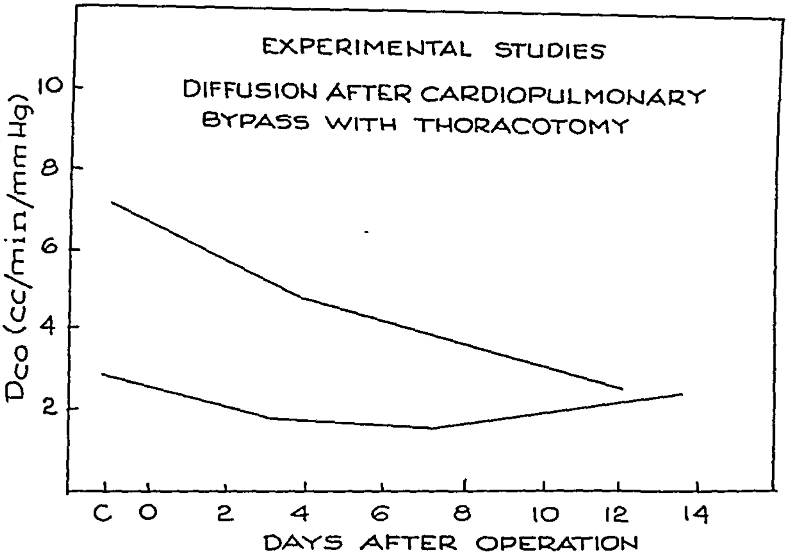

Fig. 5.—Carbon monoxide diffusing capacity before and after cardiopulmonary bypass with right thoracotomy in the dog.

pulmonary capillary bed. Conclusive evidence regarding this could be determined by measuring the pulmonary artery pressure and the cardiac output postoperatively. If there is a progressive reduction in the size of the available pulmonary capillary bed this should be accompanied by increasing pressure in the pulmonary artery or a decrease in cardiac output or a combination of these two factors.

It is probable that the observed reduction in D_{CO} is due, at least in part, to an alteration in the characteristics of the alveolo-capillary membrane itself. Several factors must be considered of etiological significance. Among these are the prolonged inhalation of high concentrations of oxygen, the use of positive pressure during anesthesia, mechanical trauma to the lungs from handling, drying, etc., and factors introduced in the technique of perfusion. It is recognized that injury to the pulmonary membrane does occur, as detailed in the reports of Kolff[6] and Muller[7] and their associates. The histologic lesions described by Dodrill[8] probably also fall in this category of injury secondary to the technique of perfusion or possibly to agents employed in perfusion. This would not, however, account for the decreased diffusing capacity observed after thoracotomy alone and it is probable that other factors related to operations within the thorax are at least as important in this regard as overloading of the pulmonary circulation during perfusion. All of these factors relating to alterations in the pulmonary membrane and in pulmonary blood flow are susceptible to evaluation; however, such studies would be difficult to carry out in human beings since exercise and sampling of mixed venous blood would be necessary.

The difference observed between these patients and patients spontaneously developing an alveolar capillary block are of more immediate interest and importance. It is characteristic of patients with alveolar capillary block that hyperventilation, particularly alveolar hyperventilation, is present. This is presumably due to hypoxemia and is mediated through stimulation of the chemoreceptor system. Because of the greatly increased diffusibility of carbon dioxide, these patients invariably have a reduced pCO_2. In the patients of this series in whom measurements were performed, using 0.1 per cent carbon monoxide in room air, definite hypoxemia was present, corresponding to the depression in D_{CO}. The response of these patients to hypoxemia was ineffectual. It should be emphasized that alveolar ventilation was normal or at least very near the preoperative measurement for the individual, yet there were a need and a stimulus for the development of hyperventilation, but this did not take place. The cause for this failure of response is not clear. It may be due to reflex inhibition of respiration by stimuli arising from the incision and from the areas of pleuritis. There may be additional inhibition of the chemoreceptor system by narcotics. Another possibility that must be considered is that some form of reversible damage to the chemoreceptor system has occurred as a direct result of operation or of perfusion.

Since interference with diffusion after operation may be severe and since it has been demonstrated to be entirely reversible, proper management of these patients during the period of maximum depression is important This particular group of patients was selected for study because of the fact that they had tolerated their operative procedure well and were convalescing satisfactorily, the lone exception being patient No 2 It is probable that these changes occur to an even more marked degree in those patients in whom respiratory inadequacy is evident postoperatively It would appear that treatment should involve elevation of the partial pressure of oxygen in the alveoli and that this could be accomplished by decreasing the dead space, by the administration of high concentrations of oxygen, and by increasing the tidal volume Decrease in the dead space can be effected by means of tracheostomy and the delivery of an increased tidal volume can be accomplished by use of respirators, particularly those designed to deliver a specific tidal volume These measures while the best available for treatment of postoperative hypoxemia, must be employed with reservation until their effects on cardiac output, pulmonary blood flow and the alveolar capillary membrane in postoperative patients are known

SUMMARY

The diffusing capacity of carbon monoxide has been studied in 7 patients before and after open intracardiac operations, in 1 patient after closed mitral valvulotomy, and in 1 patient after transthoracic repair of a hiatus hernia Depression of D_{CO} followed all of these operations in the immediate postoperative period After the intracardiac procedures, this depression persisted for 6 to 14 days There was a rapid return to a normal D_{CO} in the patient undergoing hiatal herniorrhaphy

The effect of thoracotomy alone, cardiopulmonary bypass alone, and thoracotomy with cardiopulmonary bypass was studied in a group of dogs All animals demonstrated an immediate postoperative reduction to D_{CO} and this appeared to be of longer duration in the animals additionally subjected to cardiopulmonary bypass Cardiopulmonary bypass alone was followed by no consistent changes in the D_{CO}

The desirability of determining the relative contribution of membrane damage and altered pulmonary circulation to the diffusion defect is evident The inadequacy of patient response to this defect is striking Therapy consists in reducing dead space, administration of high concentrations of oxygen, and increasing the tidal volume

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DISCUSSION

DR. JOHN H. GIBBON, JR., Philadelphia, Pa.—I can't let this nice paper go without making some remarks. As usual, it is an excellent study from Dr. Creech's group.

It is a field which has interested me for quite a number of years. I believe that postoperative pulmonary dysfunction after cardiopulmonary bypass accounts for a good deal of morbidity and mortality.

It appears to me, as Rubin Lewis sitting beside me said, that the depression of pulmonary diffusion lasts about as long as the respiratory excursions are limited by the pain of the operative wound. There is no paralysis of the diaphragm. There is no accumulation of blood or air in the pleural cavity, but there is limitation of respiratory activity from pain, lasting about 8 to 10 days. I wonder whether this depression of CO_2 diffusion doesn't parallel the period of wound healing. A nice check would be to do a lower abdominal laparotomy and see whether the same interference with CO_2 diffusion occurs.

I would like to again congratulate the authors on a very excellent paper.

DR. JOHN C. JONES, Los Angeles, Calif.—I would just like to ask the authors if they employed the use of helium with oxygen in the treatment of any of these patients. Would it not be worth while trying?

DR. GEORGE W. WRIGHT, Cleveland, Ohio.—Those of you who have never had to work with this technique probably don't appreciate the difficulties and the obstacles that one has to overcome in such a study.

I am interested in asking the authors what the range of variation is for this technique in their hands in normal individuals, and certainly in the preoperative group. When we were developing this method we found that we were unable to repeat duplicate runs with better than about a 10 to 15 per cent variation. I think this will have some bearing on the magnitude of the changes shown in this study, but I don't want to infer that this would bear on the direction of change.

DR. EDWARD J. BEATTIE, JR., Chicago, Ill.—I enjoyed this very excellent presentation.

There is one comment that I would like to add. Dr. Archer Gordon, when working in our laboratory, studied patients having major abdominal surgery, over a period of several days postoperatively. He found that although the patient was doing well clinically, most of the patients in the course of 48 hours postoperatively had arterial oxygen saturations of 90 per cent or below. I do not believe that this problem is confined to chest surgery.

DR. SCHRAMEL (Closing).—I should like to thank Drs. Gibbon, Jones, Wright, and Beattie for their comments.

To answer Dr. Gibbon, it is certainly true that this does parallel the healing of the wound and this could represent a total reduction of lung volume. However, alveolar ventilation was normal in these patients, and we have no definite evidence as to the over-all size of the alveolar capillary membrane after operation, other than this study. It is possible that reducing the area on the basis of splinting could occur.

Dr. Jones, we did not use helium in any of these patients postoperatively.

Dr. Wright, our range of normal in these patients—we used essentially the same levels as observed by you. Our variation on preoperative determinations in the same individuals runs about 10 to 15 per cent. The direction of variation, as you pointed out, however, was all in the same way, all downward, and I think if you just moved the whole thing up or down 15 per cent it wouldn't make a great deal of difference

We have not conducted these measurements in patients after abdominal surgery.

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DISCUSSION

DR. JOHN H. GIBBON, JR., Philadelphia, Pa.—I can't let this nice paper go without making some remarks. As usual, it is an excellent study from Dr. Creech's group.

It is a field which has interested me for quite a number of years. I believe that postoperative pulmonary dysfunction after cardiopulmonary bypass accounts for a good deal of morbidity and mortality.

It appears to me, as Rubin Lewis sitting beside me said, that the depression of pulmonary diffusion lasts about as long as the respiratory excursions are limited by the pain of the operative wound. There is no paralysis of the diaphragm. There is no accumulation of blood or air in the pleural cavity, but there is limitation of respiratory activity from pain, lasting about 8 to 10 days. I wonder whether this depression of CO_2 diffusion doesn't parallel the period of wound healing. A nice check would be to do a lower abdominal laparotomy and see whether the same interference with CO_2 diffusion occurs.

I would like to again congratulate the authors on a very excellent paper.

DR. JOHN C. JONES, Los Angeles, Calif.—I would just like to ask the authors if they employed the use of helium with oxygen in the treatment of any of these patients. Would it not be worth while trying?

DR. GEORGE W. WRIGHT, Cleveland, Ohio.—Those of you who have never had to work with this technique probably don't appreciate the difficulties and the obstacles that one has to overcome in such a study.

I am interested in asking the authors what the range of variation is for this technique in their hands in normal individuals, and certainly in the preoperative group. When we were developing this method we found that we were unable to repeat duplicate runs with better than about a 10 to 15 per cent variation. I think this will have some bearing on the magnitude of the changes shown in this study, but I don't want to infer that this would bear on the direction of change.

DR. EDWARD J. BEATTIE, JR., Chicago, Ill.—I enjoyed this very excellent presentation.

There is one comment that I would like to add. Dr. Archer Gordon, when working in our laboratory, studied patients having major abdominal surgery, over a period of several days postoperatively. He found that although the patient was doing well clinically, most of the patients in the course of 48 hours postoperatively had arterial oxygen saturations of 90 per cent or below. I do not believe that this problem is confined to chest surgery.

DR. SCHRAMEL (Closing).—I should like to thank Drs. Gibbon, Jones, Wright, and Beattie for their comments.

To answer Dr. Gibbon, it is certainly true that this does parallel the healing of the wound and this could represent a total reduction of lung volume. However, alveolar ventilation was normal in these patients, and we have no definite evidence as to the over-all size of the alveolar capillary membrane after operation, other than this study. It is possible that reducing the area on the basis of splinting could occur

Dr. Jones, we did not use helium in any of these patients postoperatively

Dr. Wright, our range of normal in these patients—we used essentially the same levels as observed by you Our variation on preoperative determinations in the same individuals runs about 10 to 15 per cent The direction of variation, as you pointed out, however, was all in the same way, all downward, and I think if you just moved the whole thing up or down 15 per cent it wouldn't make a great deal of difference

We have not conducted these measurements in patients after abdominal surgery

CLINICAL RESULTS OF CORRECTION UNDER HYPOTHERMIA OF ATRIAL SEPTAL DEFECTS AND PULMONARY VALVULAR STENOSIS

Earle B. Mahoney, M.D., James A. Manning, M.D. (by invitation), James A. DeWeese, M.D. (by invitation), and Seymour I. Schwartz, M.D. (by invitation), Rochester, N. Y.

THE METHODS for surgical correction of intracardiac lesions have undergone a rapid transition from the initial blind or closed methods to the present-day open heart procedures utilizing cardiopulmonary bypass with extracorporeal circulation. The initial open heart procedures were made possible by general hypothermia which results in reduced body metabolism and allows circulatory occlusion for limited periods of time without brain damage.[1, 2] The use of hypothermic techniques has not enjoyed widespread acceptance, primarily because of the short time allowed for intracardiac manipulation and the danger of refractive ventricular fibrillation. In spite of these potential difficulties, a number of surgical centers have been enthusiastic advocates, and they have reported highly acceptable series of operations using this technique.[3, 4, 5] The technique is now used primarily for the correction of pulmonary valvular stenosis, atrial septal defects of the secundum type, and for the less complicated varieties of abnormal pulmonary venous drainage usually associated with high atrial septal defects. The present trend, however, in many centers is to employ cardiac bypass techniques for all intracardiac procedures. The purpose of this paper is to review the clinical effectiveness of the hypothermic technique which we have used and, in particular, to assess the surgical problems involved and the long-term clinical results.

CLINICAL MATERIAL

During the past 3½ years, 35 patients have had, under hypothermia, repair of atrial septal defects, pulmonary valvular stenosis, and partial anomalies of the pulmonary venous return. These patients will be considered in two groups: first, valvular pulmonic stenosis, and second, atrial septal defects.

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Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

Valvular Pulmonic Stenosis.—Nineteen patients have had pulmonary valvulotomies. Three of these had significant ostium secundum defects with left-to-right shunting, and 1 had a partial anomaly of the venous return, with the right pulmonary veins draining into the right atrium. Fourteen patients were in the pediatric age range from 5 to 14 years, and 5 were adults from 19 to 37 years. All patients had definite symptoms; the most common were decreased exercise tolerance with fatigability and dyspnea with exertion. Intermittent palpitation, chest pain, and cyanosis were present in several. One girl of 19 years had termination of a pregnancy because of shortness of breath, before being referred for evaluation. One man of 30 years of age had frank congestive heart failure.

The patients were all well developed except 1. All patients had a palpable systolic thrill high along the left sternal border and a long harsh systolic murmur. All patients had a markedly diminished or absent pulmonary second sound. The fluoroscopic examination revealed a prominent active pulmonary conus and enlargement of the right ventricle in all patients. The 3 patients with atrial septal defects had increased pulmonary blood flow, and the remainder had relatively clear lung fields. The electrocardiograms showed right axis deviation and right ventricular hypertrophy in all. In general, the degree of right ventricular hypertrophy was most marked in those patients having the highest pressure gradient across the pulmonary valve. Preoperative cardiac catheterization was performed on all patients. The pullback pressure records were considered typical of valvular stenosis, and operation was advised if the right ventricular pressure was 100 mm. Hg or more.

Auricular Septal Defect.—Sixteen patients have had closure of auricular septal defects by the open technique under hypothermia. These are in addition to the 3 patients classified under pulmonary valvular stenosis, who had atrial septal defects closed at the time of pulmonary valvulotomy, and the patient who had correction of anomalous pulmonary venous drainage. One of the 16 had an associated significant pulmonary stenosis and correction of both defects. Twelve patients were in the pediatric age range, between 5 and 14 years, and 4 were adults of 23, 31, 33, and 38 years of age. All patients had significant symptoms; those of pediatric age have had growth retardation, many have had fatigability with exertional dyspnea, frequent lower respiratory infections, and intermittent cyanosis with exertion or during respiratory infections. The physical findings conformed well with those described by Taussig.[8] In general, they have been of asthenic habitus and have appeared underdeveloped and undernourished. None of the patients was cyanotic at rest. Eight, or 50 per cent, had precordial prominence. The only patient with a significant precordial thrill had an associated pulmonary valvular stenosis. The systolic murmur varied from a Grade 1 to a Grade 3 of medium pitch, and usually was heard best from the second to the fourth interspaces at the left sternal border and transmitted [illegible]
16 had soft mid-diastolic murmurs along the left stern

Fluoroscopy revealed significant cardiomegaly in all 16 patients except the 1 with pulmonary stenosis. All patients had a prominent right atrial shadow and enlargement of the right ventricle; all had an enlarged full pulmonary conus with increased pulmonary vascularity and intrinsic arterial pulsations. There was no evidence of an enlarged left atrium or left ventricle in any patient. The electrocardiographic findings were as follows: 11 had right axis deviation, 4 a normal axis, and 1 a left axis deviation. Only 4 patients had clear-cut electrocardiographic evidence of right ventricular hypertrophy; 3 of these had right ventricular hypertension of 67 mm. Hg, 55 mm. Hg, and 58 mm. Hg, respectively, and the fourth had an associated pulmonic stenosis with a right ventricular pressure of 75 mm. Hg. All others had a focal bundle branch block over the right precordium, a so-called rsR′ pattern. Ten patients had prolongation of the P-R interval, and 1 had first degree heart block. Five patients had prominence of the P wave as evidence of right atrial dilatation. No patient had evidence of left ventricular hypertrophy.

Preoperative cardiac catheterization was performed on all patients, and all had a significant left-to-right shunt at the atrial level, varying from 1 L./min./M.^{2} to 12.7 L./min./M.^{2} No patient had evidence of a right-to-left shunt or arterial unsaturation; no patient had evidence of a subauricular shunt.

Indication for operation has been the combination of (1) significant symptomatology, (2) cardiomegaly, and (3) a left-to-right shunt exceeding 1.5 L./min./M.^{2} The 1 patient operated on who had a 1 L./min./M.^{2} shunt had, in addition to the atrial septal defect, definite pulmonary valvular stenosis.

TECHNIQUE OF SURGICAL PROCEDURE UNDER HYPOTHERMIA

The operative technique is essentially the same as we have described previously,[7] and is similar to that described by others.[3, 4, 5] It includes perfusion of the coronary circulation with warm, heparinized oxygenated blood during the period of inflow-tract occlusion. Following induction of anesthesia and insertion of an endotracheal tube, the patient is surface cooled in a tub of ice water to a rectal temperature of about 32.5° C. and placed on the operating table over the warming blanket (Therm-o-rite*). The blanket is usually used to prevent excessive downward temperature drift rather than for further cooling, and we prefer to do the intracardiac procedure at a rectal temperature of about 30° C. and preferably when the temperature is beginning to rise. An anterior bilateral thoracotomy has been used most frequently, entering the right chest through the fourth interspace and the left through the third, with division of the sternum by V osteotomy. Recently, pulmonary valvulotomies have been performed by a longitudinal sternal splitting incision, and atrial septal closures have been perfo gh a right thoracotomy. The pericardium is widely opened, and vae are dissec within the pericardium so that tapes may be passed about them for inflow occlusion. Entrance into the heart or pulmonary artery is gained as follows: The venae cavae are occluded and, after allowing about 20 seconds for cardiac emptying, the pulmonary artery and aorta are occluded with a Satinsky clamp placed through the transverse cardiac sinus. A curved needle (Fig. 1) is placed in the aorta between the clamp and the aortic valve for coronary perfusion. The atrium or pulmonary artery is then opened between previously placed stay sutures. Egress from the heart is accomplished by flooding the atrium or pulmonary artery with saline and applying a noncrushing clamp to the walls. *Immediately thereafter, the aortic clamp and the superior vena* cava is released. If heart action is satisfactory, the inferior vena cava is next opened.

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*Therm-o-rite Products Company, Buffalo, N

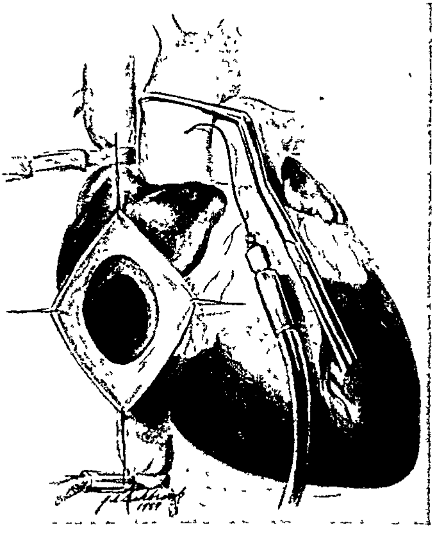

Fig 1—The technique of coronary perfusion and the exposure for closure of atrial septal defects

Coronary Artery Perfusion During Inflow-Tract Occlusion.—We consider this to be a very important adjunct to intracardiac surgery under hypothermia. Coronary perfusion has been discussed by Spencer,[4] Mahoney,[7] Riberi,[8] and others, and its value in the experimental animal has been reported from this laboratory.[9, 10] The details of the experimental study have been reported elsewhere but, in brief, the results were as follows: during inflow-tract occlusion, the pH of coronary sinus blood decreases, and the lactic acid content increases, indicating a rapidly developing myocardial acidosis. If coronary perfusion with warm, oxygenated heparinized whole blood is then begun, the pH of coronary sinus blood returns to normal, and the lactic acid content returns to pre-occlusion levels (Fig. 2). If coronary artery perfusion is started at the outset of inflow-tract occlusion, the pH of coronary sinus blood and lactic acid content is maintained at pre-occlusion levels (Fig. 3).

Oxygenated blood for coronary perfusion for the earlier cases was obtained by warming the arm of a donor and drawing venous blood in heparin.[11] We encountered considerable variation in the oxygen saturation of the blood obtained in this manner; therefore, we have abandoned this method in favor of a technique of so-called "coronary autoperfusion." Fresh heparinized venous blood is drawn from donors the morning of the operation and infused into the patient's vein, while an equal amount of arterial blood is taken from the patient's aorta by direct needle puncture after the chest has been opened. Thus, complete oxygen saturation of the blood for coronary perfusion is assured. The volume of coronary perfusion during pulmonary valvulotomy has varied from 100 to 400 c.c., and the mean average was 1.9 c.c./min./Kg.; for

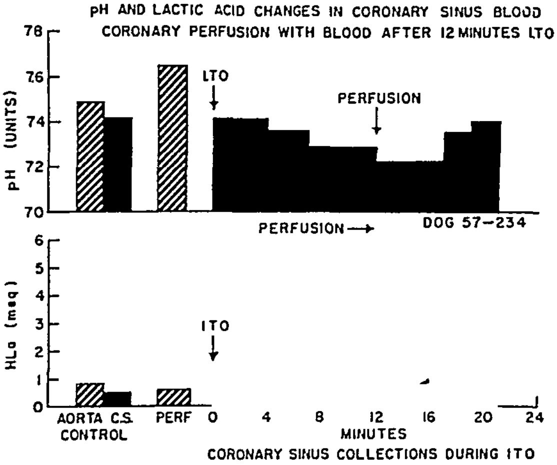

Fig. 2.—Inflow-tract occlusion with coronary artery perfusion.

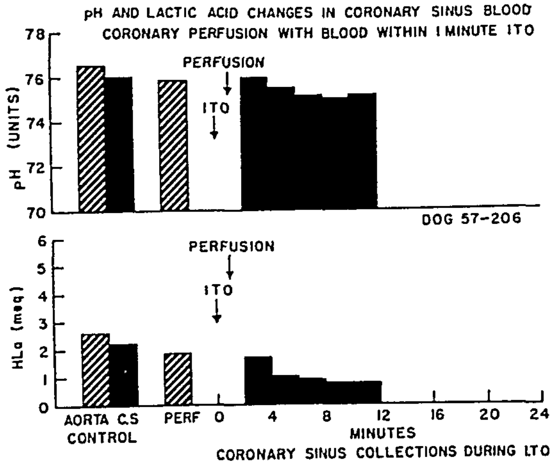

Fig. 3.—Inflow-tract occlusion with coronary artery perfusion.

closure of atrial septal defects, it varied from 175 to 500 c c, with an average of 1 5 c c/min/Kg The period of inflow tract occlusion for pulmonary valvulotomy has been between 3 and 4 minutes, and for atrial septal defects usually between 5 minutes and 7 minutes, the longest being 13 minutes

The operative findings in pulmonary valvular stenosis were characterized by an enlarged muscular right ventricle and post stenotic dilatation of the pulmonary artery at the point where the jet of blood through the stenotic valve impinged upon its wall[12] The valvular stenosis was most often due to a funnel shaped, cone-like fusion of the valve leaflets The cone might be quite long with thin walls (Fig 4) or short and thickened at its tip The opening was usually only 2 to 3 mm in diameter The commissures are not as clearly defined in congenital pulmonary valvular stenosis as they are in aortic valvular stenosis, but they can at times be defined and the cuts made accurately in the commissures Usually two cuts were made converting to a bicuspid valve, but we have the clinical impression that less insufficiency may result if three cuts are made (Fig 5) The tip of the cone has been excised if it shows fibrous thickening Three patients presented a flattened fibrous diaphragm, and in 1, two tiny openings were present (Fig 6) Blount[13] has stated that the thickened fibrous valves occurred in older patients, but this has not been a uniform finding in our patients as this thickening occurred in younger individuals with a very high degree of stenosis

The most common type of atrial septal defect encountered has been the secundum defect of the septum primum[14], or as designated by Swan,[7] a foramen ovale defect due to a defect in the valvular foraminis ovalis or complete absence of the valvula The high defects of the septum secundum usually have no cephalic margins, and are most frequently associated with anomalous pulmonary venous drainage All of these defects have an adequate margin of septum caudally, and we have purposefully avoided repair of primum defects of the septum primum or endocardial cushion defects by the hypothermic technique The technique of closure is similar to that described by others[3 5] After careful inspection of the atrial cavity, and after locating the site of entrance of pulmonary veins, the venae cavae, and coronary sinus, stay sutures of No 3 0 silk are placed at either end of the defect and tied, thus converting the oval defect to a slit The cephalad suture is then continued caudally as an over and over stitch, finally tied to the caudal stay after the left atrium has been allowed to fill with blood Several interrupted sutures are usually inserted for reinforcement The correction of anomalous pulmonary veins is usually readily accomplished by suturing the ventral margin of the septum to the right of the entrance of the pulmonary veins, thus creating a larger left atrium It may be impossible to divert pulmonary veins entering high in the vena cava Following closure of the defect, the right atrium is allowed to fill with blood and is usually flooded with saline before applying a noncrushing clamp to the atrial wall The right atrium is closed with a continuous suture

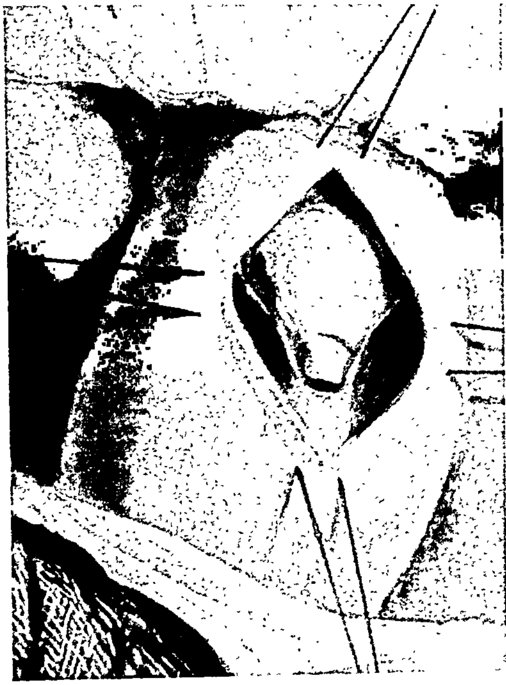

Fig. 4.

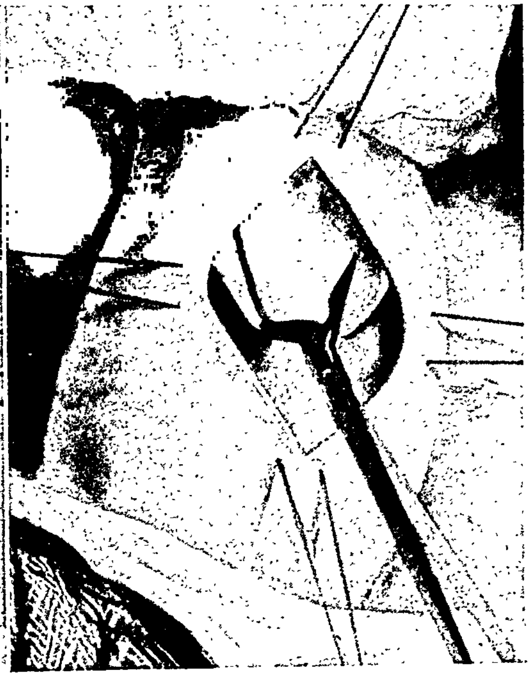

Fig. 5.

Fig. 4.—Exposure for pulmonary valvulotomy.
Fig. 5.—Technique of pulmonary valvulotomy.

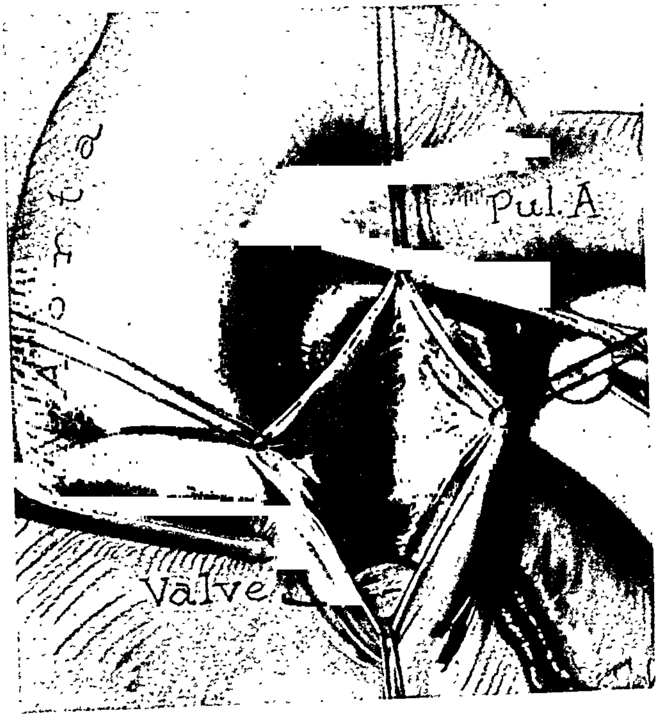

Fig. 6.—Diaphragm type of pulmonary valvular stenosis.

Patients having both pulmonary stenosis and atrial septal defect have had both abnormalities corrected at the same operation. The valvulotomy is performed first, and the circulation is re-established for about 20 minutes to allow cardiac recovery. The atrial septal defect is then repaired during a second period of inflow tract occlusion.

OPERATIVE COMPLICATIONS

Pulmonary Valvular Stenosis.—There have been no operative or postoperative deaths. One patient, a 33 year old man, developed ventricular fibrillation which was successfully converted to sinus rhythm. Twenty-one months previously, he had had a transventricular[15] pulmonary valvulotomy performed with a minimal decrease in right ventricular pressure. Coronary artery perfusion was not used and, after 6 minutes of inflow tract occlusion, ventricular fibrillation developed when the inferior vena cava was opened. Cardiac arrest was induced by re-establishing inflow-tract occlusion and, after cross-clamping the aorta, 19 c.c. potassium chloride solution (1 mEq./c.c.) was injected into the coronary circulation. Circulation was maintained by massage and, after 3 minutes, the heart became responsive and 20 c.c. of 50 per cent glucose was injected intravenously. This was followed by a spontaneous effective ventricular beat and soon thereafter a sinus rhythm (method described by Mavor and his associates[16, 17]). The patient's postoperative course was uneventful. There were no other operative complications in this group of patients.

Atrial Septal Defects.—There was one operative death due to ventricular fibrillation, and 2 other patients developed this operative complication, but it was successfully converted with potassium and glucose. The first patient in this series did not have coronary perfusion during 5 minutes of inflow tract occlusion, and fibrillation began while the atrium was being closed. Patients 6 and 8 had coronary perfusion with blood from a "warmed donor arm" and, in both instances, the perfusate was desaturated. Patient 6, a 6 year old girl, began to fibrillate while the defect was being closed. The closure was completed, and defibrillation was successfully accomplished with potassium and glucose. Technical difficulties were encountered in Patient 8 which required 13 minutes of inflow tract occlusion. Fibrillation began 3 minutes after circulation was restored, and attempts at conversion were unsuccessful in spite of both electrical shock and administration of potassium with glucose. No ventricular arrhythmias occurred when coronary perfusion was carried out with fully saturated arterial blood. Six patients had atrial fibrillation during some period of cardiac manipulation, but this caused no difficulty and reverted spontaneously.

POSTOPERATIVE COMPLICATIONS

The patients in both groups required only the usual postoperative support necessary for any thoracotomy. No problems of either postoperative bleeding or thrombosis were encountered and, in general, the postoperative period was remarkably benign. One patient developed an unsuspected psychiatric difficulty after doing well in the postoperative period. She subsequently died of pneumonia, and is the one late death in the series.

CLINICAL RESULTS

Pulmonary Valvulotomy.—These patients have been followed for a varying period of from 2 months to 42 months. Those who have been followed for more than 6 months have all become asymptomatic. The 1 patient who had frank cardiac failure before operation is now 17 months postoperative, and has no evidence of failure, does not require digitalis, and is able to work full time. The clinical course, the electrocardiogram, and pulmonary valve pressure gradient data are tabulated in Table I. All patients have shown significant reduction of right ventricular hypertrophy by electrocardiogram, 13 actually have no residual right ventricular hypertrophy 10 months to 2 years following operation, and 4 patients maintain 1+ right ventricular hypertrophy at 17 months to 37 months.

TABLE I. CLINICAL RESULTS—VALVULAR PULMONIC STENOSIS
(*THE SEVERITY OF CLINICAL SYMPTOMS AND THE RIGHT VENTRICULAR HYPERTROPHY AS TABULATED ON A BASIS OF 0 TO 4+*)

PATIENT	AGE AT OPERATION (YEARS)	LENGTH OF FOLLOW-UP (MO.)	CLINICAL COURSE		ELECTROCARDIOGRAM		RV—P. ART. SYSTOLIC GRADIENT (MM. Hg)	
			PRE	POST	PRE	POST	PRE	POST
1. R. W.	13	42	2+	0	3+ RVH	Normal	150	15
2. R. T.	7	40	4+	0	4+ RVH	Normal	167	14
3. R. G.	33	37	1+	0	3+ RVH	1+ RVH	106	—
4. W. S.	14	36	2+	0	4+ RVH	1+ RVH	153	10
5. K. K.	11	34	1+	0	2+ RVH	Normal	91	7
6. G. B.	36	31	1+	0	2+ RVH	1+ RVH	140	19
7. R. D.	6	28	2+	0	3+ RVH	Normal	164	24*
8. R. W.	6	26	2+	0	2+ RVH	Normal	110	10
9. C. F.	7	24	1+	0	3+ RVH	Normal	125	15
10. D. K.	19	23	2+	0	2+ RVH	Normal	97	—
11. C. W.	5	21	2+	0	4+ RVH	Normal	173	11
12. D. M.†	6	18	1+	0	2+ RVH	Normal	85	16
13. J. F.	12	17	1+	0	3+ RVH	Normal	102	9
14. C. O.	30	17	2+	0	3+ RVH	1+ RVH	200	10*
15. J. D.†	7	16	1+	0	3+ RVH	Normal	105	25
16. N. H.	6	15	1+	0	2+ RVH	Normal	100	16
17. M. G.†	6	10	2+	0	2+ RVH	Normal	100	16
18. D. B.	37	3	1+	0	2+ RVH	1+ RVH	66	9*
19. J. D.	5	2	2+	0	3+ RVH	1+ RVH	165	62*

*Operating room pressure recording.
†Associated auricular septal defect.

The pressure gradient across the pulmonary valve has been determined by preoperative catheterization, before and immediately after valvulotomy in the operating room, and by catheterization 1 year postoperatively. The first 5 patients operated on by the open technique had an immediate reduction in the right ventricular pressure to near normal levels at operation. The sixth patient had a minimal reduction in spite of what had impressed us as a typical valvular obstruction and a satisfactory valvulotomy At that time, we were fearful that an associated infundibular stenosis had been missed The immediate postoperative gradient was 150 mm Hg, but catheterization 1 year later revealed a gradient of only 10 mm Hg This situation has been encountered in 6 patients (Fig 7), and all have had a satisfactory reduction in the pulmonary valve gradient when studied 6 months to 1 year later[18] The data on patients having immediate regression of the gradient are compared with those having late regression (Fig 8), and the end result is the same with near normal pressure relations between the right ventricle and pulmonary artery The patients having the gradual decrease in right ventricular pressure have also had a slower regression of electrocardiographic evidence of right ventricular hypertrophy

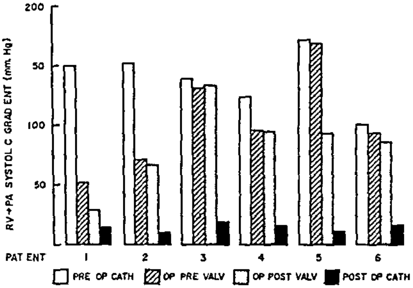

Fig 7—Late regression of right ventricular pulmonary artery pressure gradient in patients having hypertrophy of the right ventricular outflow tract

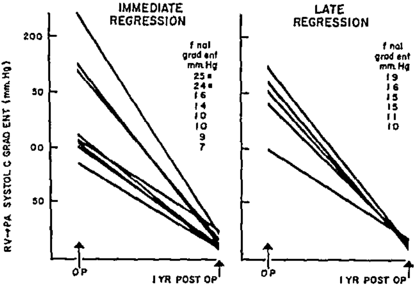

Fig 8—Right ventricular pulmonary artery pressure gradients following valvulotomy

Reversible Outflow Tract Hypertrophy of the Right Ventricle—Fig 9 shows the normal outflow tract of the right ventricle portrayed by the cine fluorographic technique of angiocardiography[19] View *A* shows the outflow tract at the end of systole, and *D* early in systole Fig 10 is the same view of the outflow tract in a patient with pulmonary valvular stenosis exposed at comparable times during systolic ejection of the radiopaque material. During late systole, the hypertrophied infundibulum causes marked narrowing of the outflow tract, but it does expand during maximum systolic ejection. Those patients who do not have an immediate reduction in right ventricular pressure

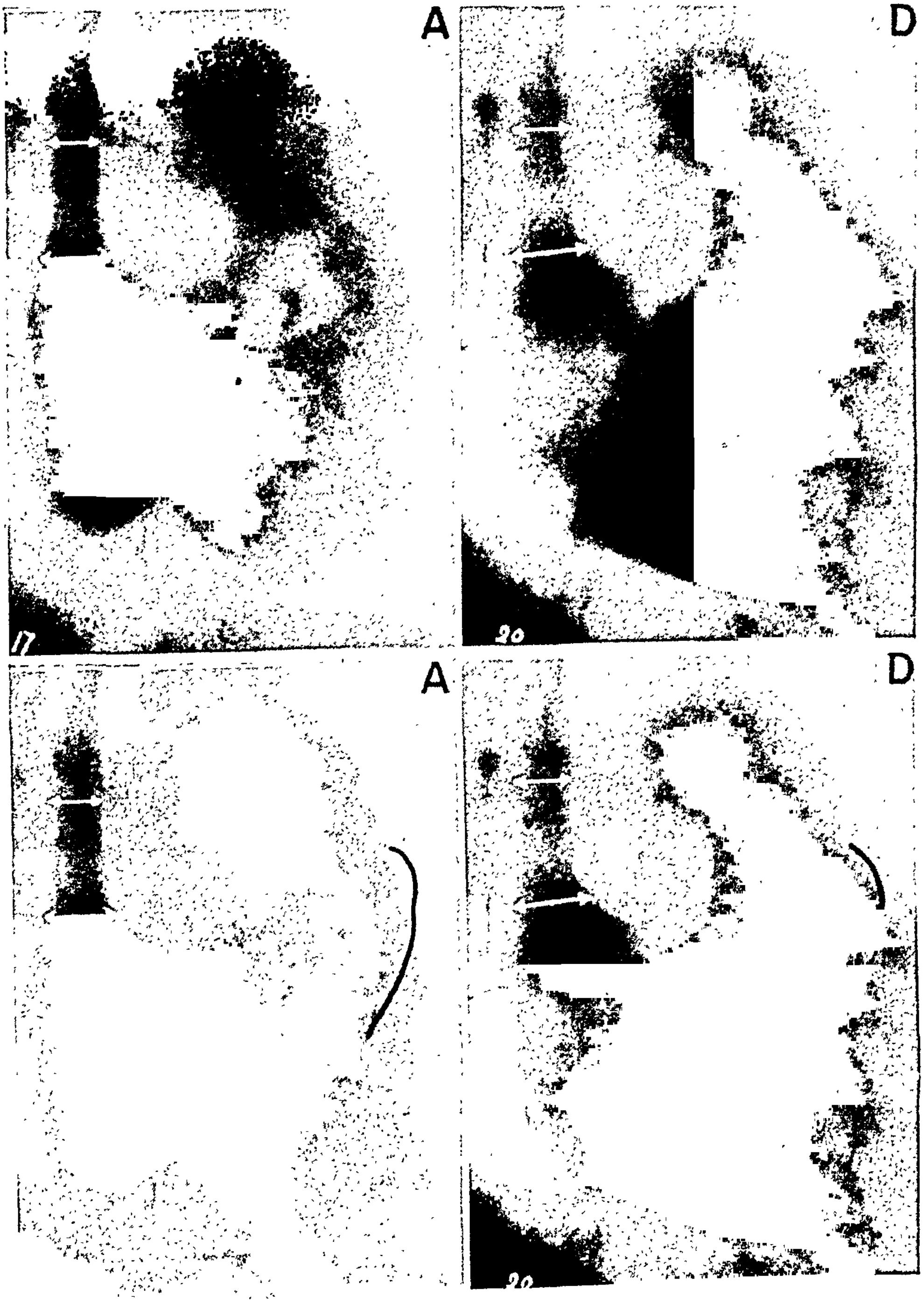

Fig. 9.—Cine-an showing normal outflow tract of right ventricle.

after valvulotomy have a markedly contractile muscular and hypertrophied infundibulum. If the operator's finger is inserted through the valve, into the outflow tract, a very firm contraction is noted during systole. This differs, however, from a true infundibular stenosis in that there is no fixed fibrous band or inexpansile area of outflow obstruction.

Atrial Septal Defects.—None of the surviving 14 patients has had postoperative symptoms (Table II). All have had marked reduction in the cardiothoracic ratio 1 year following operation. Fluoroscopic examination indicates a return to normal pulmonary vascularity. Nine patients who have had postoperative catheterization had complete closure of the defect, with no evidence of a left-to-right shunt and no right heart hypertension. Those not yet catheterized have had a rapid increase in growth and development and a marked decrease in physical findings, although a soft murmur may still persist, even though the defect is completely closed. One 12-year

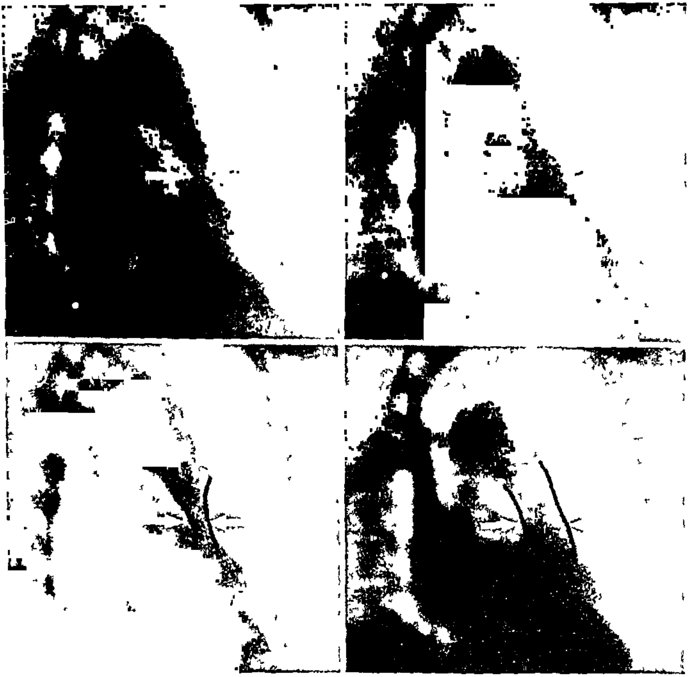

Fig 10 —Cine-angiocardiogram showing right ventricle outflow tract in patient with pulmonary valvular stenosis

ed 15 pounds since *operation, has no symptoms, and has had a significant* ease in heart size. She does, however, have a hyperactive precordium and ɜ residual increase in pulmonary vascularity, so there may still be a small lual left-to-right shunt.

TABLE II. CLINICAL RESULTS—AURICULAR SEPTAL DEFECTS

TIENT	AGE AT OPERATION (YEARS)	LENGTH OF FOLLOW-UP (MO.)	CLINICAL COURSE		CARDIO-THORACIC RATIO		LEFT-TO-RIGHT SHUNT (L./MIN./M.^{2})	
			PRE	*POST*	*PRE*	*POST*	*PRE*	*POST*
M. A.	14	32	2+	0	.55	.45	4.5	0
C. M.	5	28	3+	0	.60	.48	3.5	0
L. D.*	12	28	2+	0	.45	.40	1.0	0
J. D.	5	28	2+	0	.58	.50	2.3	0
R. W.	31	22	2+	0	.52	.50	12.7	—
D. L.	6	21	2+	0	.55	.45	3.5	0
J. S.	6	20	2+	0	.60	.48	3.2	0
M. F.	12	Operative death	2+	—	.55	—	6.2	—
W. R.	12	18	3+	0	.58	.52	5.5	
D. R.	13	16	1+	0	.54	.45	2.3	0
C. W.	23	12	2+	0	.50	.48	5.3	0
S. M.	10	12	2+	0	.50	.48	2.9	
M. S.	38	3 wk. postop. death	2+	—	.50	—	5.5	—
E. V.	7	9	3+	0	.55	.50	5.0	
R. H.	9	6	2+	0	.55	.49	8.5	
E. A.	33	4	2+	0	.52	—	—	

*Associated pulmonic stenosis.

DISCUSSION

The hypertrophy of the right ventricular outflow tract, which has been rved in association with pulmonary valvular stenosis, presents an interɩg problem. When we first found little or no decrease in the right venılar pressure following an adequate valvulotomy, we presumed that an ndibular obstruction had been overlooked even though such an obstruccould not be defined by finger palpation. The patient had a favorable ical course, and cardiac catheterization 1 year later revealed a marked in right ventricular pressure and a minimal gradient across the pulmo- valve. Five other patients have had well-documented evidence of gradudecreasing pressure gradients following valvulotomy. The angiocardions and the clinical course of these patients indicate that a physiological ertrophy of the outflow tract may develop as the result of purely valvular ıosis and that, after the valvular obstruction is overcome, the hypertrophy resses.

The combination of pulmonary valvular stenosis and infundibular stenocoexisting in the presence of an intact ventricular septum has been dissed by numerous authors. McGoon and Kirklin[20] estimated that the two associated in about 25 per cent of the cases, and they found infundibular ıosis more often present in older children and adults with valvular stenosis. lboys[21] had 6 patients who required infundibular resection in conjunction with valvulotomy. Certainly, the presence of pure infundibular stenosis without a ventricular septal defect and without pulmonary valvular stenosis is quite rare. Our experience has indicated that muscular hypertrophy can simulate an infundibular obstruction, but that it is possible to differentiate the two preoperatively and at the operating table. Needless resection of the wall of the outflow tract can thus be avoided.

The results of pulmonary valvulotomy by an open technique appear superior to the results obtained by the closed transventricular technique. Blount[13] estimated an over-all mortality rate of 10 per cent of operations by the transventricular route reported in the literature and a 5 per cent mortality by the open technique. There have been no fatalities in the group reported here, but the total number of operations is not large. The right ventricular pressure usually regresses to a near normal level after open valvulotomy, and the gradient across the pulmonary valve is usually less than 20 mm. Hg. The average right ventricular pressure in this series is 33 mm. Hg, with an average gradient of 14 mm. Hg. One possible disadvantage of the open technique is the danger of pulmonary valvular insufficiency.[22] Five patients have postoperative diastolic murmurs along the left sternal border, and 1 patient has hemodynamic evidence of pulmonary insufficiency with a pulmonary artery pressure of 29/2 mm. Hg. No patients have evidence of clinical problems secondary to this, nor have they developed electrocardiographic evidence of right ventricular hypertrophy or of increase in heart size. Many years of observation will be necessary to evaluate this aspect of the problem.

Our clinical experience confirms the value of coronary artery perfusion with oxygenated whole blood. The amount of whole blood used for perfusion is less than normal coronary blood flow; but at reduced temperatures, the low flow rate is adequate to prevent myocardial anoxia and acidosis in the experimental animal and in the human patient. During inflow-tract occlusion without perfusion, the heart rate gradually slows, and the myocardium becomes cyanotic. The electrocardiogram deteriorates, and frequently the heart requires massage when circulation is re-established. This is undoubtedly the most dangerous period from the standpoint of ventricular fibrillation. In contrast with this, during coronary perfusion, the myocardium remains pink, the rhythm is regular, and the electrocardiographic changes are minimal. When circulation is restored, the heart action is usually vigorous, and the systemic arterial pressure is maintained at the pre-occlusion level of that degree of hypothermia. The beneficial effect of the neostigmine used by Swan[2] is, in part, due to a slowing of the heart and, thus, a reduction in metabolic demands of the myocardium.

The most obvious disadvantage of the open heart procedures performed under hypothermia is the limitation in time available for intracardiac manipulation. The method should be limited to the procedures described, plus possibly open valvulotomy for congenital aortic stenosis, although cardiac bypass is probably preferable for this. Preoperative diagnosis must be accurate;

and, if there is any question of a complicated lesion requiring intracardiac correction, the technique should not be used. One of our patients who had both a pulmonary valvulotomy and closure of an atrial defect has postoperative evidence of a small ventricular septal defect which was not evident on preoperative studies, and which might have been found if cardiac bypass had been used.

It should be emphasized that the successful use of hypothermia requires careful attention to many details, but it is simpler than cardiopulmonary bypass techniques and it requires much less blood, manpower, and equipment. Our own experience persuades us to continue its use for the simpler procedures and, although readily available, to reserve the pump-oxygenator for the more complicated defects. Perhaps the greatest value of hypothermia in cardiac surgery will be its use in combination with cardiopulmonary bypass.

SUMMARY

A review of the experience with 35 patients upon whom cardiac surgery was performed with the aid of hypothermia is presented. Nineteen patients underwent pulmonary valvulotomy, and 16 had closure of atrial septal defects by open technique. The physical findings and indications for operation are presented for each of these 2 groups of patients. The technique for surgical correction of the lesions, including the application of coronary artery perfusion during inflow-tract occlusion, is outlined. The clinical results are evaluated both in the immediate postoperative period and after long-term follow-up. Catheterization data are presented, and particular attention is directed to the reversibility of the outflow-tract hypertrophy of the right ventricle associated with valvular pulmonic stenosis.

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DISCUSSION

DR JULIAN JOHNSON, Philadelphia, Pa —I would like to emphasize again the value of intermittent occlusion under hypothermia If you get in a spot where you can't complete your suture within the 5 or 6 minutes which you have allotted yourself, there is no reason why you can't back out, let the heart recover, and then go back in at a second period

We have used this successfully We have limited our hypothermia to 90° F and have not had inflow occlusion for more than 4 or 5 minutes Even without coronary perfusion we have had virtually no difficulty under these circumstances We have set 4 minutes as our goal, but if we find that we can complete our suture within another half minute or so we are apt to go ahead and finish But if it is apparent that we are going to take more than 4½ or 5 minutes, we stop, take the clamps off, let the blood run through the heart for 10 minutes, and then go back for a second period We have had virtually no difficulty with this since we have put these limitations on ourselves

Previously when we would get in a tight spot and maybe take 8 or 9 minutes in one period of occlusion we did have trouble

DR SAFUH ATTAR, Baltimore, Md —We have used deep hypothermia to a lower degree than has been used in this presentation We have brought our patients down to 26° C and so far we have not had any untoward effect in the sense of frequent ventricular fibrillations in which we could not revert the rhythm back to normal

However, we have had unusual complications, and this is the reason for my coming up here, to inquire whether you have had similar ones We used this technique for the correction of pulmonary stenosis and atrial septal defects in the same situations as stated by the authors However, we encountered the complication of peroneal palsy in 3 cases This was detected immediately after the operation and had to be treated in the usual manner There was no definite evidence of any pressure on the peroneal nerve as the hypothermia was being used

I would like to address the question whether the deep hypothermia of the nerve, since we brought the temperature down to 26° C, could have caused the peroneal palsy

DR. MAHONEY (Closing).—I would like to thank the gentlemen who discussed and asked questions with regard to the paper.

So far as Dr. Johnson's *intermittent occlusion is concerned*, we have used this, of course, ourselves. We feel that we can be allowed between 7 and 8 minutes of occlusion time, using coronary perfusion with the oxygenated whole blood. But on numerous occasions we have had to do intermittent occlusion and we feel it is a very worth-while thing to do. Of course we do it when doing both a pulmonary valvulotomy and an atrial septal defect on the same patient.

In regard to the second discusser's questions, our temperatures are as a rule between 30° and 31° C. rectal at the time of the inflow tract occlusion. We have not had any nerve palsies as a result of hypothermia to our knowledge. I doubt very much whether the hypothermia itself had to do with the peroneal palsy, although I am not sure.

I would like to emphasize that one must pad these patients extremely well and be very careful about pressure points, else one gets into severe difficulties as a result of the cold, particularly if one is using a blanket.

SIMPLIFIED TECHNIQUE FOR DIRECT VISION PULMONARY VALVOTOMY

Conrad R. Lam, M.D., and Rodman E. Taber, M.D., Detroit, Mich.

THERE is general agreement at the present time that if the surgeon is to make the best possible correction of pulmonic valve stenosis, he must be able to see what he is doing. This principle, however, has been given reluctant acceptance by some surgeons, including the senior author,[1, 2] because the transventricular method popularized about 10 years ago by Brock[3, 4] had many attractive features. First of all, it was the only operation available at that time as an alternative to the shunt operations which were soon found to be contraindicated in pulmonic stenosis with intact ventricular septum.[5, 6] It could be performed rapidly, if necessary, the valve of a dying, cyanotic infant could be opened within 10 minutes of the time of the skin incision. The mortality of the operation was low. In the series of 75 patients operated upon at the Henry Ford Hospital before June 1, 1957 (when our present method was adopted as a routine procedure), there were only three deaths and one of these was in an infant only a week old.

The immediate clinical results of the transventricular operation appeared to be satisfactory. For example, the first patient in our series, operated upon in May, 1950, showed immediate reduction in heart size and was in good health 8 years later. The second patient had a right ventricular pressure of 70 mm. Hg before the operation, 6 months later it was down to 30 mm. Hg. Clinical examination of this patient 7 years later revealed a normal heart size.

The technical aspects of the operation were made easier by the introduction of new instruments, notably the adjustable valvulotome of Potts and his associates,[7] and the modification of the Bailey mitral valve guillotines, which were especially useful in adult patients.[8]

However, as early as the 1953 meeting of this Association, several members rose to point out that the transventricular operation was not uniformly satisfactory.[9, 10] In a considerable number of cases, postoperative catheterization of the right heart had shown that right ventricular pressures were not sufficiently reduced or an immediate reduction had not been permanent.[12] At this meeting, Dodrill[13] reported a successful case of open pulmonic valvotomy, in an operation utilizing right heart bypass and autogenous lung oxygenation.

From the Division of Thoracic Surgery of the Henry Ford Hospital, Detroit, Mich.

Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

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artery. There is no reason to put on such a clamp, since there is no back pressure in the lung to cause retrograde flow and no aspirating action which might cause air to be taken in.

Traction sutures are placed with an atraumatic needle at the proximal and distal ends of the proposed incision into the pulmonary artery. An atraumatic type of clamp is then placed longitudinally to exclude the portion of the artery for the incision. This maneuver is facilitated by the post-stenotic dilatation which almost invariably accompanies pulmonic valve stenosis. The artery is incised and additional traction sutures are placed to retract the two lips of the incision. The vena caval snares are tightened and the anesthetist is asked to give notification of the passage of 1 minute of time.

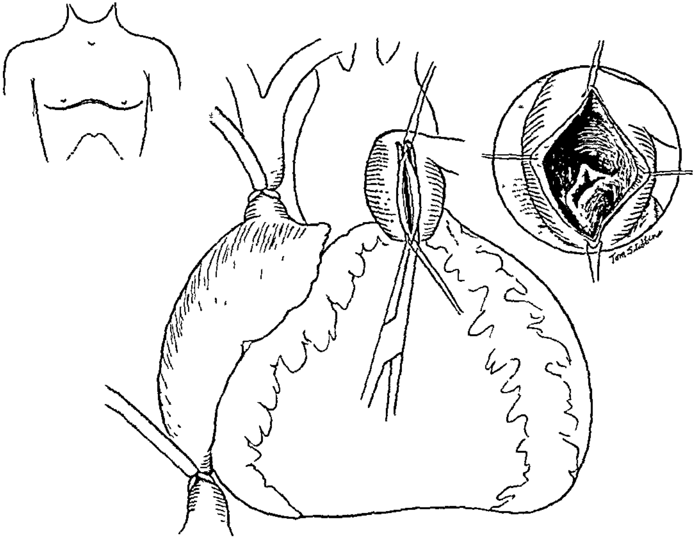

Fig 1.—Method of exposure of the pulmonary valve for direct vision valvotomy without hypothermia. Note that no occluding clamp is placed on the pulmonary artery distal to the incision.

Restoration of the circulation after 1 minute is considered to be desirable, and, after 2 minutes, mandatory. The maximum period of occlusion in our series has been 1½ minutes, although obviously the occlusion period may be repeated an indefinite number of times with periods of normal circulation intervening. Following occlusion of the venae cavae, the heart is allowed to beat several times to empty the right side, and the pulmonary artery clamp is removed. An assistant places a vein retractor at the proximal angle of the incision. The blood in the artery is aspirated and, as soon as possible, if the size of the valve orifice permits, the tip of the aspirator is placed in the right ventricle for a few seconds. Note is then made of the type of valve and the indicated valvotomy performed. If there is no sign of commissures in the typical dome-shaped valve with severe stenosis, incisions are made anteriorly and posteriorly out to the arterial wall (Fig. 2). It is useful to have the first assistant, who stands on the left side of the table, grasp one side of the valve with a forceps while the surgeon holds the other side. If there are actual commissures or rudimentary ones, the incisions are made carefully along the commissural lines. Pulmonic insufficiency is an unnecessary sequel to open pulmonic valvotomy. Finally, a finger is introduced through the opened valve into the ventricle to verify the patency of the entire outflow tract. In 1 case, a narrow fibrous band of subvalvular stenosis was noted, and this was cut away during a second period of caval occlusion. It is to the credit of our pediatric diagnostic team (Dr. R. F. Ziegler and Dr. Edward Green) that no instance of infundibular stenosis appeared in patients scheduled for open valvotomy. We consider that the problem in infundibular stenosis with intact ventricular septum is so complicated that cardiopulmonary bypass is indicated.

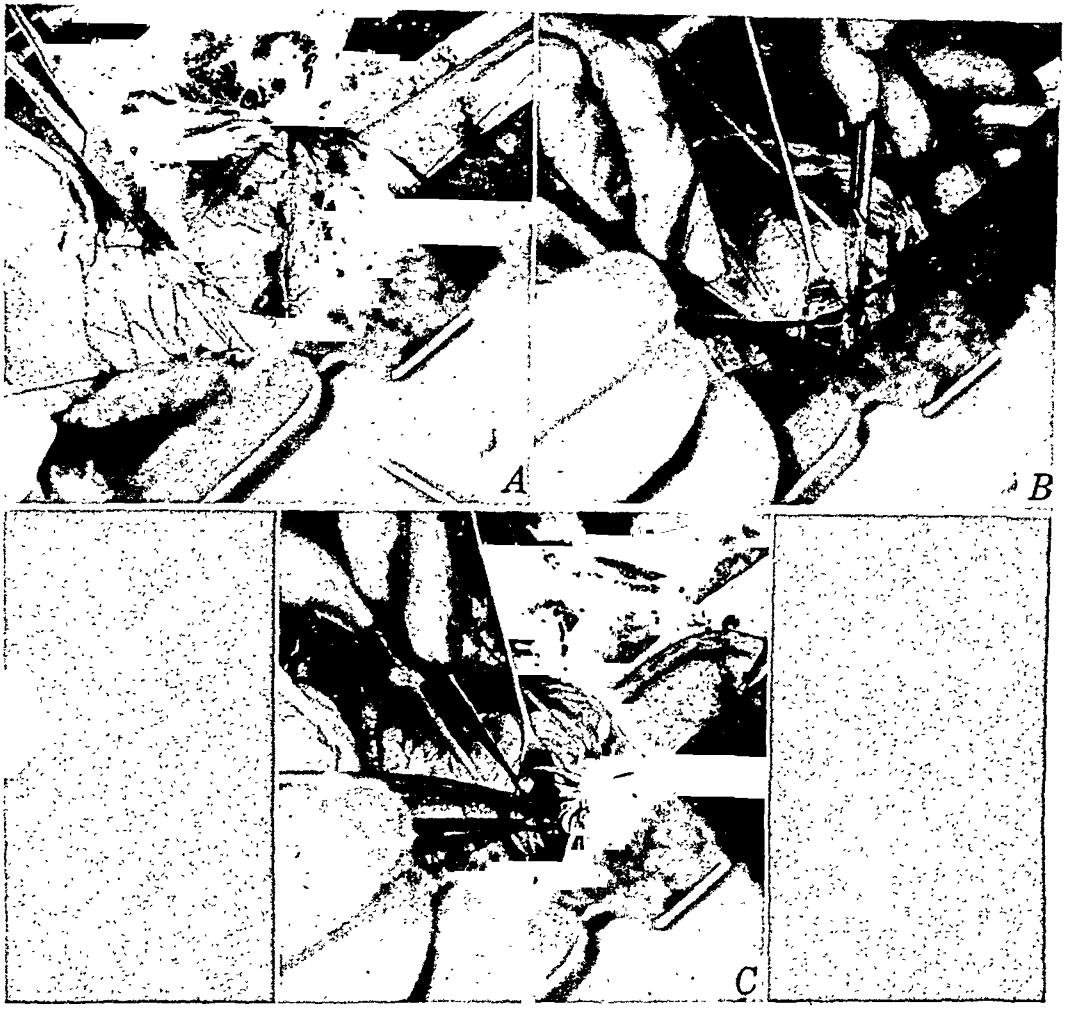

Fig. 2.—Photographs of a typical pulmonary valvotomy. *A*, The artery has been incised in a portion excluded by a longitudinally placed clamp. *B*, Removal of the clamp reveals the dome-shaped deformed valve. *C*, The valve has been opened by anterior and posterior incisions.

Following the ventricular exploration, the superior vena caval snare is released and, in a few seconds, blood is ejected from the right ventricle. In the meantime, the lips of the pulmonary artery incision have been held up with the traction sutures and, as the artery fills and overflows with blood, the clamp is closed about the incision. There has been no suggestion of air embolism in our series. The arterial incision is then closed with 5-0 silk, placed as a continuous horizontal mattress type of suture, reinforced by returning with an over-and-over suture, after which the clamp is removed. The pericardium is sutured loosely, the right side of the chest is drained into a water-seal bottle, and the chest is closed in the conventional manner. Only rarely has there been sufficient blood loss or other factors, such as preoperative anemia, to make a transfusion necessary.

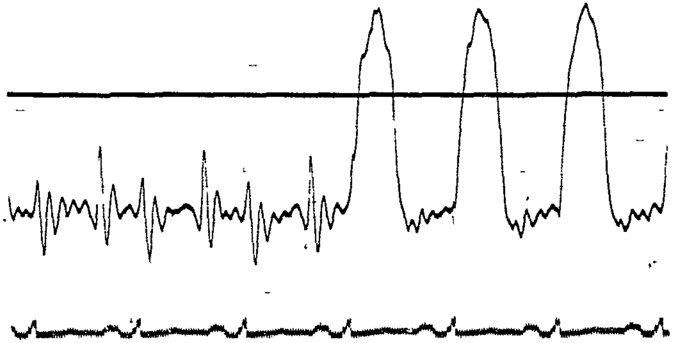

Fig 3.—Pressure tracing at catheterization of the right heart, showing the typical picture of pure valvular stenosis The low pressure in the pulmonary artery on the left may be compared with the high pressure of the right ventricle on the right.

RESULTS

Since June, 1957, 49 patients have been scheduled for open pulmonary valvotomy by this technique. In 48 patients, the proposed valvotomy was carried out. There was 1 case in which there had been a gross error in diagnosis and there was no significant pulmonary stenosis; this case will be discussed later. There was a wide age range. Eight patients were between the ages of 1 and 3 years, 27 were from 3 to 10, 4 from 20 to 30 years, and 3 were over thirty. The oldest patient was 47 years of age.

There was one postoperative death; this occurred in the youngest patient in the series, a child 18 months of age. Although the increased risk of operation at this age was appreciated, it was evident that immediate relief of the severe pulmonic stenosis was indicated. The child was first seen at the age of 6 months and was catheterized. The right ventricular pressure was 110/6 mm. Hg and the pulmonary artery could not be entered. Ten months later, a second catheterization showed that the ventricular pressure had risen to 170/0. At open valvotomy, it was found that the valve had a tiny opening which would barely admit a small aspirator tip. Valvotomy was carried out to produce a bicuspid valve in the usual manner. The finger could not be passed through the valve ring, but a dilator indicated that no localized infundibular stenosis existed. The postoperative course was stormy, with abdominal distention on the first day and difficulties with pulmonary secretions. On the third postoperative day, tracheotomy was done to facilitate the removal of secretions. There was continued respiratory embarrassment and death occurred on the fourth day. Autopsy showed extensive atelectasis and pneumonia. The pulmonary valvotomy appeared to be adequate, but the marked hypertrophy of the entire right ventricle caused some narrowing of the outflow tract. The exact role of this relative obstruction in the fatal issue could not be stated with certainty. We are inclined to believe that when the localized valvular obstruction is relieved, the hypertrophy of the ventricular outflow tract will disappear and with it the tendency to obstruction.

There has been no important problem of postoperative complications in the other 47 patients. In the short period of follow-up observations, clinical studies have indicated an excellent correction of the defect in every patient. In several cases, the murmur has disappeared and in all there has been a reduction in heart size and electrocardiographic evidence of less right ventricular hypertrophy. Naturally, with the experience with the transventricular operation in mind, there may be skepticism about the long-term results until there have been a number of postoperative catheterizations. One patient, aged 47, had a preoperative right ventricular pressure of 100/0 mm. Hg and a pulmonary artery pressure of 35/0, giving a gradient of 65 mm. Hg. Postoperative catheterization showed a reduction of the ventricular pressure to 40/0 and a pulmonary artery pressure of 35/5, a gradient of only 5 mm. Hg.

There was one frank diagnostic error in a patient scheduled for pulmonary valvotomy which resulted in the patient's death. This occurred in a child 18 months of age. There was a systolic murmur over the pulmonary artery suggestive of pulmonic stenosis. Unfortunately, the catheterization data were interpreted as being completely confirmatory for this provisional diagnosis. No shunting at any level was demonstrated; the oxygen saturation in the inferior vena cava was 11.5 vol. per cent; in the superior vena cava, 10.8 vol. per cent; in the right ventricle, 11.2 vol. per cent; and in the pulmonary artery, 11.7 vol. per cent. The pressure in the right ventricle was 90/20-2, and the pulmonary artery pressure was 16/2. In retrospect, there were some danger signals, but these were not noted in time to prevent the fatality.

At operation, it was evident that post-stenotic dilatation of the pulmonary artery was absent. When the exclusion clamp was applied to the pulmonary artery, the heart action rather promptly became poor. It was thought that the clamp was occluding the stenotic valve orifice in some way. Also, it was noted that when the vena caval snares were occluded, there was not good collapse of the right auricle. A second application of the pulmonary artery clamp again resulted in cardiac difficulty. The decision was made to open the artery during caval occlusion without the use of the clamp. Pink blood came out of the ventricle The pulmonary valve showed little if any stenosis, although token cuts were made at its commissures The clamp was replaced and suturing of the vessel was begun The heart began to fail and the suture line was rapidly completed Intermittent cardiac compression was begun quickly and this reversed the signs of cerebral anoxia, but the heart never showed any further tendency toward spontaneous beating in spite of an hour and a half of resuscitative efforts Autopsy showed two atrial septal defects, one of the secundum variety and another of the ostium primum type with *minimal deformity of the mitral valve It was evident that catheterization* had not revealed the atrial septal defects because the shunt was balanced There is no explanation for the error in determination of the gradient between the ventricle and pulmonary artery Obviously, the patient should have been scheduled for repair of the septal defects with the aid of the pump oxygenator Following this unfortunate experience, all of the data, including angiocardiograms, were carefully scrutinized and there were several things to suggest that the diagnosis was not simple pulmonary valve stenosis The typical post stenotic dilatation of the pulmonary artery was missing The lung fields were relatively clear, but were more suggestive of pulmonary resistance than diminished flow The angiocardiograms did not substantiate the diagnosis of valvular stenosis

SUMMARY AND CONCLUSIONS

It is proposed that open pulmonary valvotomy without hypothermia and without the pump oxygenator is feasible and safe Valvotomies have been carried out in 48 patients with a single mortality, which occurred in the youngest patient in the series A second fatality occurred in a patient in whom pulmonic stenosis was absent, and in whom, at autopsy, two atrial septal defects were found The operation is suitable only for pulmonic stenosis of the valvular type Differentiation of this type from isolated infundibular stenosis and other congenital defects should be possible with the diagnostic techniques available to the cardiovascular team

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DISCUSSION

DR. HENRY SWAN, II, Denver, Colo.—I would like to compliment Dr. Lam on his usual level of presentation of his material. It is always extremely interesting and vivid, the way Conrad can tell you what he does.

I merely rise to reaffirm our belief and confidence in the use of the open valvuloplasty for the pulmonary valve. We continue to use hypothermia because, unlike Conrad, although I admit the operation usually takes only 1½ or 2 minutes, I like to have 4 or 5 minutes available for a 2-minute operation, so that you don't feel hurried. I agree, though, that one could certainly go back after short occlusions, as Dr. Johnson has suggested and as we have done with arterial septal defects for a number of years.

Now, on the other hand, we continue to use hypothermia because in our opinion and in our practice we believe it does not add risk to the operation. The risk of hypothermia at 30° to 31° C. we feel is roughly equivalent to that of ether anesthesia, and for this reason we do not feel that it adds any risk to the operation of pulmonary valvuloplasty.

We have had experience with something over 60 patients now, and we agree with Dr. Mahoney that there is no evidence that there is actual true infundibular stenosis associated with these patients. You have a hypertrophy of the outflow tract, which does go away as measured over a period of several months, and we have yet to see our first patient who had true infundibular stenosis associated with valvular stenosis.

As we are about to discuss with you in the next paper, we believe that one can very readily handle infundibular stenosis when it occurs as an isolated lesion and, therefore, although it is true that it is nice to be able to distinguish preoperatively, Dr. Lam, between valvular and infundibular stenosis, if you have a patient under hypothermia you are able to manage either condition with equal facility. So that we still believe that it is desirable to have the patient under hypothermia, but we couldn't agree more that the open valvuloplasty is the best approach to this condition.

DR. DONALD B. EFFLER, Cleveland, Ohio.—I, too, would like to congratulate Dr. Lam for his presentation. It appears that the operative time is getting longer—Dr. Lam took 1 minute, Dr. Swan took 4 minutes, and now I propose a method that takes much longer. At the Cleveland Clinic we advocate surgical treatment of valvular pulmonic stenosis utilizing extracorporeal circulation with the pump-oxygenator. Our numerical experience is about the same as that described by Dr. Lam. We use cardiac bypass for several reasons. First of all, we, too, were displeased with the long-term results that followed the closed methods of pulmonary valvulotomy. Second we recognize the possibility of diagnostic error, or inadequacy of diagnosis. In severe cases it may be very difficult to distinguish between infundibular obstruction of the right ventricular outflow tract from tight valvular stenosis. Dr. Lam has already mentioned his experience with the diagnostic error that resulted in a surgical fatality. The third reason, and perhaps the most important, is our experience with pulmonary valvulotomy alone. We have been more and more impressed by the significant gradient that results from pulmonary valvulotomy even when it is performed under direct vision. With total cardiac bypass it is our practice to complement valvulotomy by incision of the annulus and the distal outflow tract of the right ventricle itself. In this way the surgeon can assure himself that there is no obstructing moderator band or infundibular lesion proximal to the stenosed valve; even then relief of the gradient is not complete—at least at the immediate time of surgery. However, catheterization studies performed a year after operation are rewarded by the finding of normal anatomic and physiologic function.

Perhaps there is a basic difference in personality and nervous system that permits one surgeon to tolerate, and the other to resent, the unrelenting pressure of the ticking clock I do not question that in the hands of a gifted technical surgeon like Dr. Lam, who enjoys this sort of operation, much can be accomplished in the short space of one minute I do not question whether the operation can be done in this elapsed period of time, but I do raise the point as to whether it should be done. From the standpoint of surgical training it is my belief that this emphasis on speed constitutes some form of surgical pyrotechnics I honestly believe that the emphasis on surgical speed is a step backward rather than forward.

It reminds me of that ancient story on the correct method of kissing an ostrich Most of you will remember the graphic description of technique that is followed with the admonition, "but you've got to be quick!"

Much has taken place and has been discussed before this Society since the meeting in San Francisco a few years back. Perhaps it is well that four different approaches to the problem are still in use the closed valvulotomy of Brock, the instantaneous valvulotomy of Lam, the cold valvulotomy of Swan, and the bypass valvulotomy of Effler. Perhaps time will be the deciding factor, but it must be remembered that this is a completely correctable disease and that our goal should be 100 per cent correction with a minimal mortality rate

DR JAMES ALASTAIR KEY, Toronto, Ontario—I, too, would like to congratulate Dr Lam on his presentation

There is just one point which perhaps might be of some significance, and that is that I know Dr Lam to be a keen musician, but I think he possibly doesn't like Puccini, because he seems to have an aversion to getting either his or his tiny patients' hands frozen!

However, it is quite possible, especially in dealing with children, that the use of an air conditioned operating theater, and especially if one uses a volatile preparation for sterilization or cleansing of the skin, that Dr. Lam has been utilizing some degree of hypothermia of which he is not aware

We certainly know in children that as much as a 2° drop in temperature can occur under these circumstances during the course of opening the chest and exposing the heart. Like other discussers, it would seem to me, therefore, that the results of Dr Lam and Dr Taber indeed bear witness to their surgical dexterity. Whether they justify the abandonment of hypothermia in the treatment of direct vision pulmonary valvotomy would seem more open to question

DR WILLIS J POTTS, Chicago, Ill—It is not a particularly pleasant thing to do but occasionally it is necessary. the consumption of fricasseed crow in public The person who is going to observe this procedure with a certain amount of delight is Henry Swan.

For a number of years we employed the transventricular approach for the correction of pulmonary valvular stenosis Approximately 100 children were operated upon by this technique with one operative death The immediate results were excellent, in fact, spectacular. Since we had developed special valvulotomes and dilators for this procedure we continued to use the transventricular approach longer than we should have

We now use the open direct visualization technique under hypothermia as described by Conrad Lam We are not as fast as he, but usually complete operation on the fused valves in less than 3 minutes We still use the transventricular approach for infants with huge hearts

Because of recurrent stenosis of the valve we have had to re operate on 7 children to date and undoubtedly will have to re operate on more in the future. Although the children who required re operation were tremendously improved for some years, all symptoms returned. At the second operation the valve cusps had so completely re fused that it was impossible to see where the cusps had been separated

During the past few years we have operated upon 42 children with isolated valvular stenosis under direct vision without mortality. Whether the cusps of the valve will again fuse, even though they have been completely opened, only time will tell.

For the surgical approach we prefer a Y-shaped incision and longitudinal splitting of the sternum. A Y-shaped incision is quite satisfactory, especially for boys. If there is any criticism of the appearance of the incision the boy can be sent to Yale and have his letter before matriculation.

PRESIDENT DE BAKEY.—I suppose, if it were really known, the path on the road to truth in science is strewn with the bones of fricasseed crow.

DR. BENSON B. ROE, San Francisco, Calif.—I think that Dr. Lam's excellent presentation and the paper before him of Dr. Mahoney are worthy of further support, with the return toward the simplified techniques which we all think are desirable for the reasons so well expounded.

However, in each of these series, and in the experience of all of us, there are these unavoidable errors in diagnosis, which confront us with an embarrassing problem in the operating room. I think, therefore, we should work further toward a compromise arrangement permitting us to continue using hypothermia, but having the pump-oxygenator available, without wasting this large amount of blood.

We will hear later, I hope, more about the Edglugate blood preservative developed by Drs. Smith, Brown, and Sealy. This method permits having the blood drawn and available where it can be quickly added to the pump-oxygenator and brought into use where these diagnostic errors arise. Blood drawn and anticoagulated in this manner can be kept for several days and used for other patients if not needed for the extracorporeal circuit.

DR. GEORGE H. A. CLOWES, JR., Cleveland, Ohio.—Since people are advocating either a very quick job at normal thermic levels (Dr. Lam) or the use of the oxygenator, *taking all the time that is wanted (Dr. Effler), I would like to recommend the compromise.*

In our clinic we have found it very convenient to follow the teaching of Ivan Brown and Converse Peirce on the matter of using hypothermia with an oxygenator. I draw this to your attention because one can use a smaller oxygenator, slower blood flows which require simple cannulations, and have a very easy time of it with no rush.

We have a series of patients that have been taken down to 25° C. With external cannulations of the femoral veins and the jugular vein in the neck, the type of catheters you can easily slide into these will permit quite adequate flows and maintain very satisfactory conditions at 25°, which may amount to only a quarter of the flow that is required at normal thermic conditions to maintain pH, adequate oxygenation, and CO_2 levels where they should be.

This we have tested thoroughly in dogs and have followed in the course of Peirce and Brown to go on to do it with patients. I recommend, for those who don't like to hurry, that this may be a very satisfactory way of getting around the problem and still saving the blood.

DR. TABER (Closing).—I would just like to emphasize two points that Dr. Lam mentioned in the paper. As is the case frequently in cardiovascular surgery, the operation is as good as the diagnosis. In our experience, valvular and infundibular stenosis are an extremely uncommon combination together, and the cardiolgists have been able to ferret out the cases of infundibular stenosis and not present those to us for a closed operation.

The diagnostic techniques have not been anything, I believe, that are unusual, consisting of angiocardiography, cinefluorography, and the usual catheterization studies.

The second and final comment would be with regard to the time for the valvotomy which has been mentioned by several discussers. *I think if you were to use this technique you would* find 1 to 1½ minutes an entirely adequate period. Multiple occlusion periods are, of course, possible if needed.

THE SURGICAL TREATMENT OF ISOLATED INFUNDIBULAR STENOSIS

*Henry Swan, M D , William P Hederman, M Ch * (by invitation), Philip S Vigoda, M D ** (by invitation), and S Gilbert Blount, Jr ,
M D (by invitation), Denver, Colo*

Some difference of opinion exists concerning the relative frequency of subvalvular pulmonic stenosis with intact ventricular septum, or, as more commonly stated, isolated infundibular stenosis

Paul Wood,[1] in a series of 750 cases of congenital heart disease, found that 2 per cent or 15 cases were isolated infundibular stenosis Of all cases of pure pulmonic stenosis, he stated 4 out of 5 are valvular and 1 out of 5 is infundibular [2] On the other hand, Campbell,[3] in his series of 1,130 cases of congenital heart disease of which 113 were pure pulmonic stenosis, has seen only 2 cases of isolated infundibular stenosis, only one of which was confirmed by surgery Abbott[4] in her 1,000 autopsied cases of congenital heart disease reported only 2 cases of infundibular stenosis with closed interventricular septum

From the first description of pure infundibular stenosis by Elliotson,[5] in 1830, until 1948, when general application of cardiac catheterization came into use, only 14 autopsied cases had been reported Keith,[6] in his classic lectures on malformations of the heart, alludes to some cases of pure infundibular stenosis but the cases are not described adequately and we do not know whether any of his cases were previously reported

Since that time, most reported series of pulmonic stenosis with intact interventricular septum have a few cases of what are believed to be pure infundibular stenosis Besides the series of Wood and Campbell, already mentioned, Kjellberg[7] has reported 3 out of 25, Dow[8] 1 out of 8, Glover[9] 4 out of 25, Joos[10] 1 out of 26, Abrahams[11] 8 out of 69, Dimond[12] 2 out of 20, Kirklin[13] [14] 3 out of 19, and Van Loo and his co workers[15] reported 6 cases of infundibular stenosis of which 4 were of the isolated variety Brock,[16] in a more recent study, states that he has operated on 9 cases of infundibular stenosis as compared with

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Read at the Thirty ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles Calif April 21 23 1959

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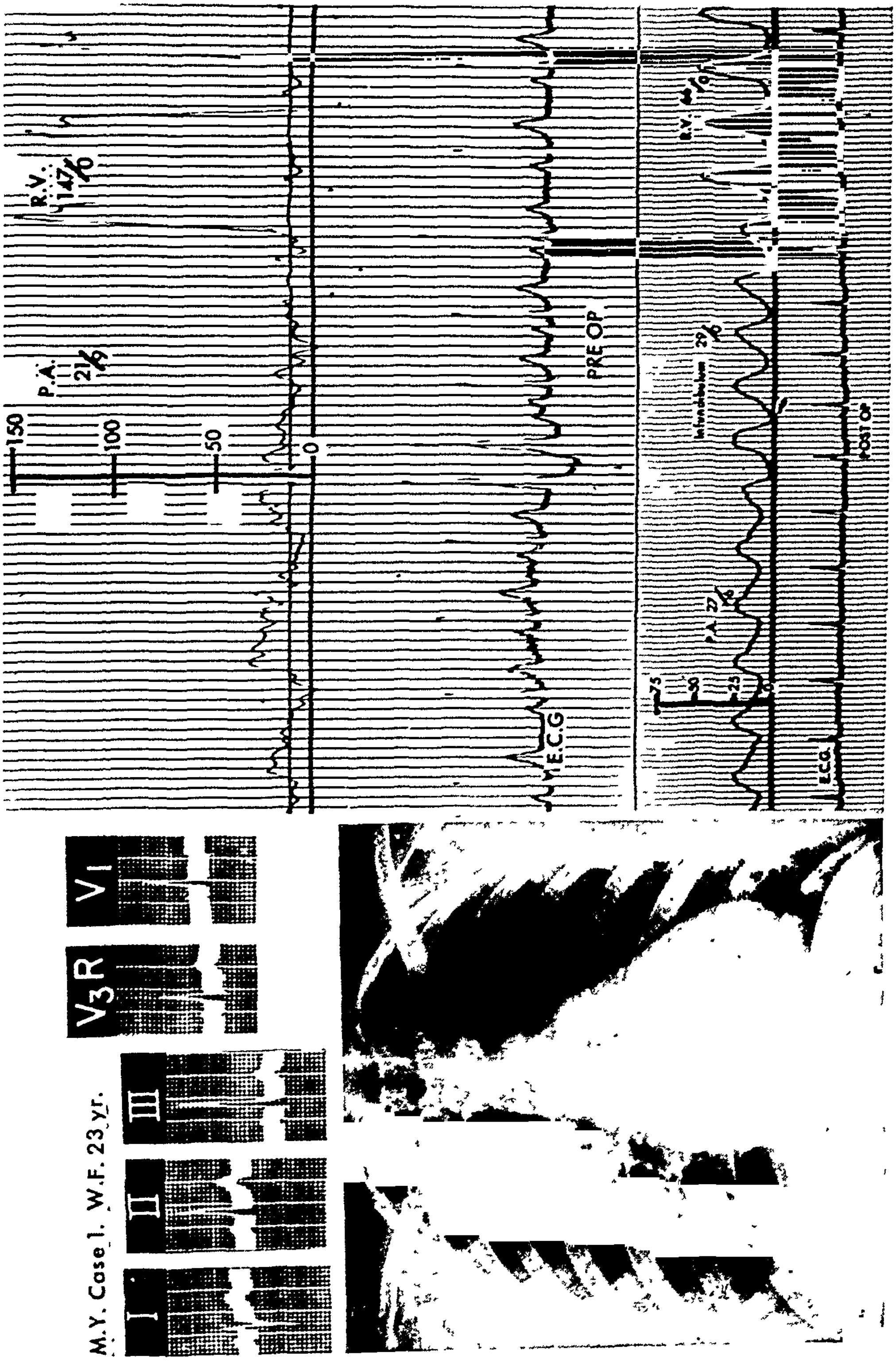

Fig. 1.—Case 1 (M. Y.), white woman, aged 23. Preoperative electrocardiogram and x-ray. Cardiac catheter tracings showing preoperative gradient of 126 mm. Hg between pulmonary artery and right ventricle and postoperative gradient of 39 mm. Hg.

111 cases of valvular stenosis. In a perusal of the literature since 1958,[17] about 60 cases of isolated infundibular stenosis have been reported The great majority of these have been diagnosed at catheterization, a small number at operation, and the least number at autopsy

We would like to report 5 cases of isolated infundibular stenosis treated surgically by outlining the operative treatment and the results

CASE REPORTS

CASE 1.—M Y, a 21 year old white mother, was seen in 1953 with a 2½ year history of dyspnea on exertion and easy fatigability, but no other symptoms A heart murmur had been detected at the age of 6 years and she had been restricted in activity by her parents However, she had had an uneventful pregnancy 2 years before admission She had had one episode of cyanosis in her youth after swimming a long distance

Physical examination revealed a healthy girl with a Grade 4, rasping systolic murmur and a thrill, both maximal in the second and third left interspaces parasternally and definitely louder in the third space than in the first The second pulmonic sound was diminished

The *electrocardiogram* revealed right ventricular hypertrophy and right axis deviation X ray studies showed a heart size within normal limits with flattening in the main pulmonary artery area

Cardiac catheterization showed a sharp fall in pressure from right ventricle to pulmonary artery, the former being 147 mm. Hg systolic and the latter 21 mm Hg systolic The actual level in the outflow tract at which this fall occurred was not noted exactly but was thought to be at the pulmonary valve Oxygen saturation determinations showed no evidence of a left to right shunt

In this first case, the preoperative diagnosis was isolated pulmonic valvular stenosis

Operation· On Nov 6, 1953, under general anesthesia, the patient was cooled to 30° C A bilateral transverse thoracotomy incision was used and, when the pericardium was opened, it became obvious that there was a definite infundibular chamber in the outflow tract of the right ventricle which was beating out of phase with the rest of the ventricle The chamber enlarged during early systole, then contracted during ventricular diastole A definite line of demarcation between the main part of the ventricle and the chamber was clearly visible and the thrill commenced at that point After inflow and outflow occlusion, the infundibular chamber was incised vertically through an area previously infiltrated with 1 per cent procaine. There was a stenotic ring at the lower end of the chamber with a 3 5 mm aperture The pulmonary valve was normal Using a punch, the ring was excised in bites until a finger could easily be passed down into the right ventricle The incision in the infundibulum was closed with interrupted mattress sutures of silk Total occlusion of circulation lasted 5 minutes and 10 seconds After this, the thrill was markedly diminished and the infundibulum now beat in phase with the ventricle

The *postoperative course* was uneventful, and when seen in July, 1954, she was asymptomatic A murmur was still present but the second pulmonic sound was now normal. An electrocardiogram revealed considerable regression of the right ventricular hypertrophy. Cardiac catheterization 8 months after operation showed a pulmonary artery pressure of 27/6 mm. Hg On withdrawal of the catheter an area of pressure of 29/0 was found and on withdrawing further into the right ventricle a jump to 66 mm Hg systolic occurred (as compared with a preoperative pressure of 147 mm Hg) No further studies have been performed to see if there has been any further change in ventricular pressure in the last 5 years (see Fig 1).

CASE 2—L H, a 9 year old white boy, had a known heart murmur since 1½ years of age At that time he had had attacks of fainting accompanied by cyanosis of the face and rigidity of the whole body. These attacks ceased at the age of 5. He had some dyspnea on

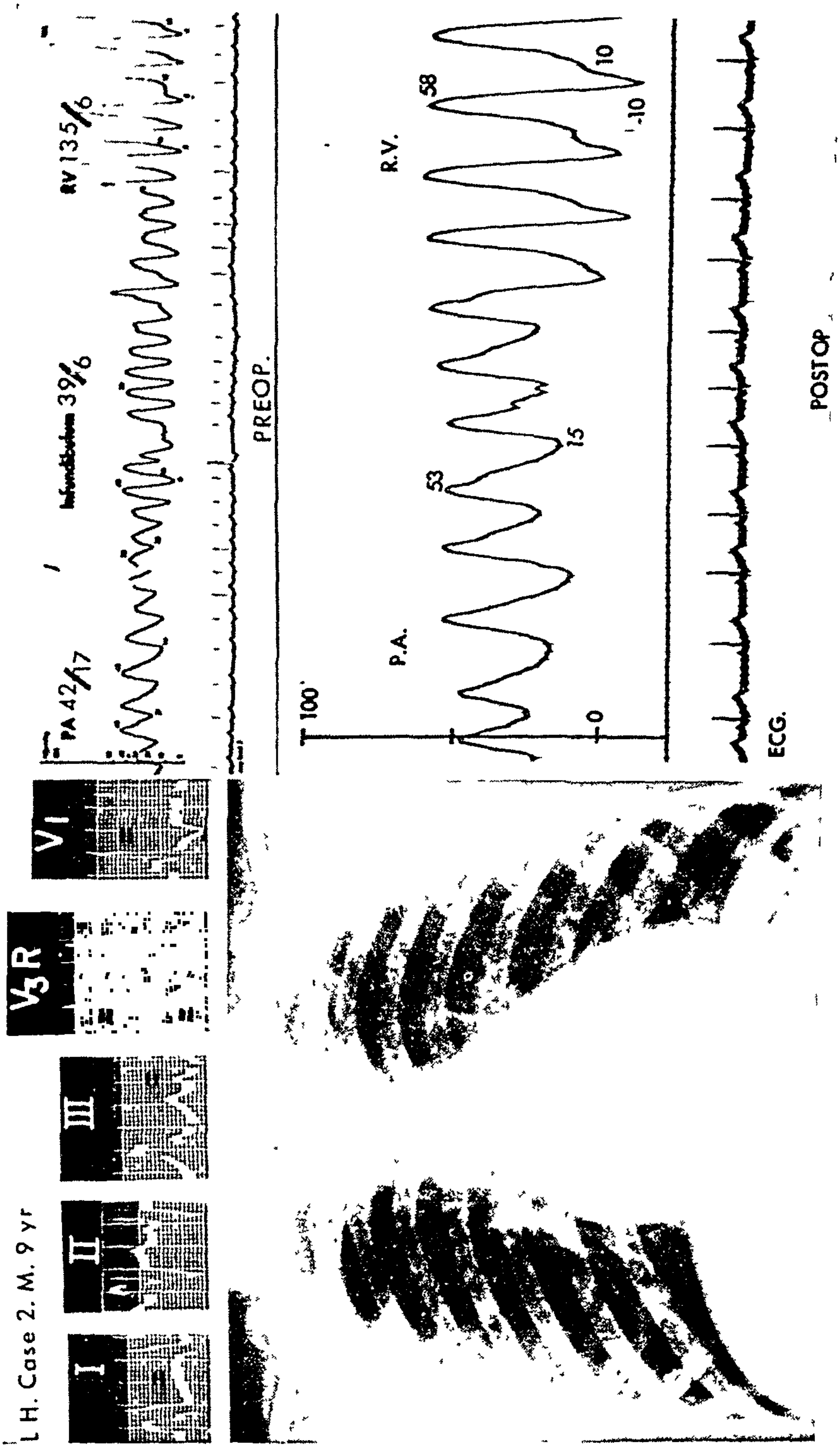

Fig. 2.—Case 2 (L. H.), 9-year-old white boy. Catheterization studies showing a typical infundibular pressure chamber and an over-all systolic gradient of 93 mm Hg preoperatively and no gradient postoperatively.

exertion and fatigability, but no squatting or cyanosis other than that mentioned. He was admitted to Colorado General Hospital because of a skull fracture on Dec. 3, 1955, and later referred to the Cardiology Department.

Physical examination revealed an undersized, chronically ill child. A slight right ventricular lift was felt along the lower left sternal border. A marked systolic thrill maximal in the second left intercostal space was palpated close to the sternum. Auscultation revealed a harsh, Grade 4 systolic murmur in the second left intercostal space which radiated to the apex and became more high pitched as one moved downward.

The *electrocardiogram* revealed right ventricular hypertrophy.

Fluoroscopy showed decreased lung vascularity with a normal aorta and a prominent main pulmonary artery. The right atrium and right ventricle were enlarged.

Cardiac catheterization, on Jan. 20, 1956, showed that the right ventricular pressure was markedly elevated at rest, 135/6 mm. Hg. The pressure in the infundibulum was only 39/6, and the pulmonary artery pressure was 40/17. The infundibular chamber appeared to extend from low in the right ventricle to the pulmonary valve. Peripheral arterial saturation was 97.3 per cent at rest and 89.8 per cent at exercise. No evidence of left to right shunt was shown by the O_2 saturation studies.

The preoperative diagnosis was isolated infundibular valvular stenosis, possibly with a right to left shunt on exercise through a patent foramen ovale.

Operation: On Jan. 24, 1956, under general anesthesia, the patient was cooled to 26.5° C. The pulmonary artery was of normal size. An obvious infundibular chamber was seen which beat out of time with the rest of the right ventricle. The vigorous thrill commenced over the infundibular chamber which was 3 mm. thick. The tight fibrous infundibular stenosis, about 3 to 4 mm. in diameter, was treated by excising a portion of crista supraventricularis, the ring of fibrous tissue, and some muscle. A finger was then passed into the main cavity of the right ventricle and no ventricular septal defect could be felt. No red blood appeared in the right ventricle during the procedure indicating that both septa were intact. A running mattress suture closed the incision during release of inferior vena caval occlusion. Total occlusion time was 5 minutes and 40 seconds. Palpation revealed no thrill remaining over the infundibulum. The patient made an uneventful recovery.

Postoperative cardiac catheterization on Feb. 15, 1956, showed that no systolic pressure gradient remained between right ventricle and pulmonary artery, the systolic pressure in each being 55 mm. Hg. The O_2 saturation studies revealed no evidence of left to right shunt. The arterial blood was fully saturated with oxygen at rest and after exercise.

Follow up observation in June, 1957, 1½ years after operation, showed the patient to be asymptomatic with no exercise intolerance. The electrocardiogram still showed some right ventricular outflow tract hypertrophy but a definite improvement had occurred. A Grade 3 murmur still remained, but the second pulmonic sound was increased. The patient no longer had pulmonic stenosis but had mild pulmonary hypertension (see Fig. 2).

CASE 3.—J. W., a 21 year old white woman, had a known heart murmur since birth, but had had no symptoms until 6 months prior to admission when she developed chills and fever and subsequently complained of easy fatigability and a considerably reduced exercise tolerance. She had had two fainting spells.

Physical examination, when she was first seen in December, 1956, revealed a marked systolic thrill and a harsh, rasping Grade 6 systolic murmur over the entire precordium, both maximal close to the sternum in the third left intercostal space. The murmur was very loud and could be heard at some distance from the chest wall. It was louder in the third than in the first intercostal space, and as loud in the fourth as in the second. A sustained thrust was felt at the lower left sternal border.

The *electrocardiogram* revealed sinus tachycardia, 138 per minute, and right ventricular hypertrophy.

Fluoroscopy showed an enlarged pulmonary trunk with normal left and right pulmonary arteries. The right side of the heart was enlarged.

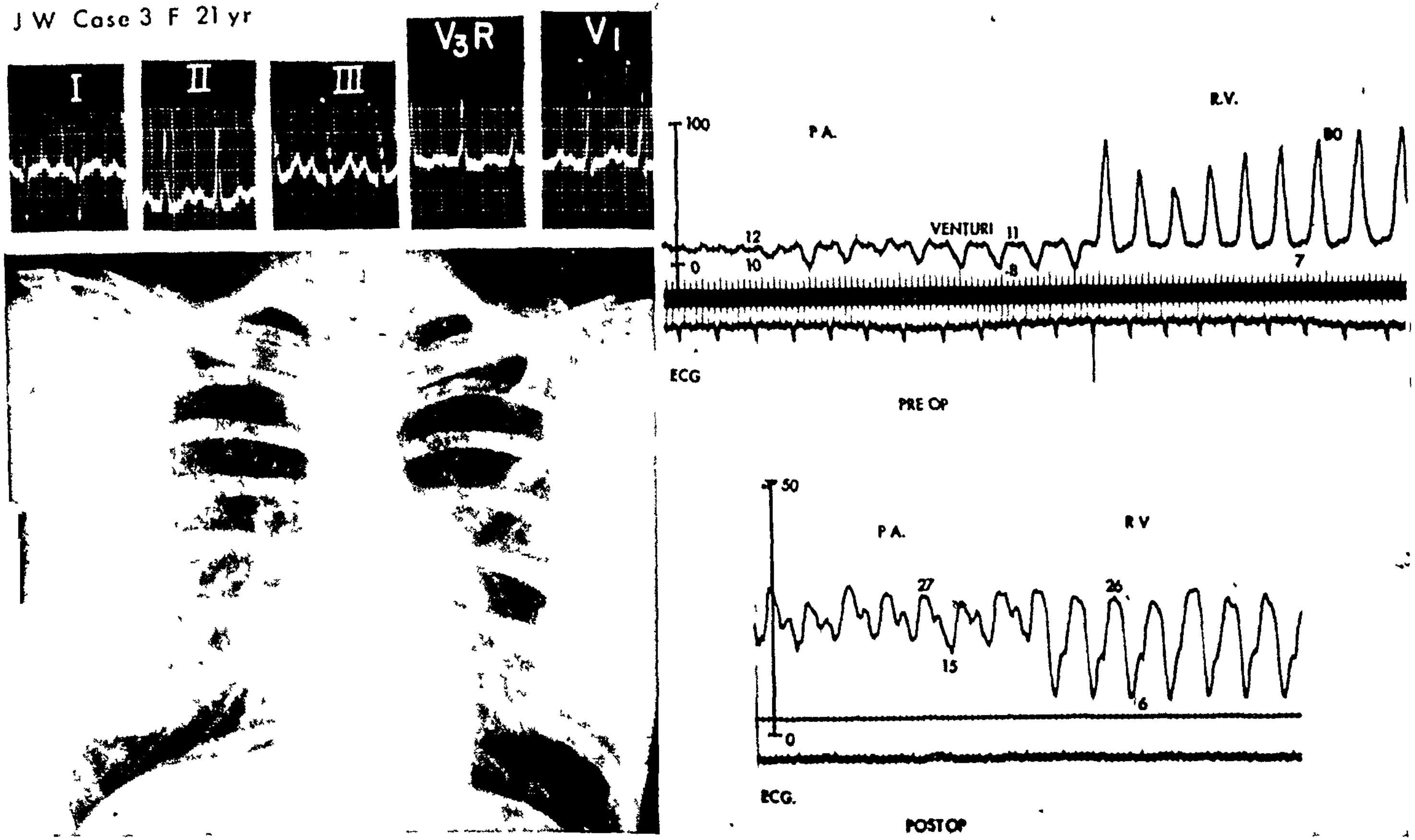

Fig 3 —Case 3 (J. W), 21-year-old white woman Preoperative studies show systolic gradient of 77 mm Hg and, in addition, a Venturi effect while postoperative pressures show no systolic gradient

Cardiac catheterization, on Dec 7, 1956, showed that the pressure in the pulmonary artery was 13/8 mm. Hg and that an abrupt rise to 90/8 mm. Hg occurred at some distance below the pulmonary valve in the infundibular region of the right ventricle There was no pressure change at the pulmonary valve, itself No evidence of a shunt or peripheral arterial O_2 desaturation was found

The preoperative diagnosis was isolated infundibular pulmonic stenosis

Operation. On Dec. 11, 1956, with the patient under general anesthesia and hypothermia, a bilateral transverse thoracotomy was used. The lungs were very pale The heart was slightly enlarged A clear cut infundibular chamber was seen distal to a line of demarcation, 4 cm below the pulmonary valve The systolic thrill was maximal in the chamber and diminished along the pulmonary artery which showed only slight post stenotic dilatation

The wall of the infundibulum was incised after inflow outflow occlusion and neostigmine bradycardia. A moderate sized chamber was entered The stenosis at the lower end admitted the tip of the index finger and was composed of a dense fibrous ring and, in addition, comprising its posterior border, was a broad band of muscle running obliquely upward across the lumen of the ventricle Using scissors and forceps, the entire ring and portions of the muscle were excised until it was possible to admit three fingers through the opening The absence of red blood in the right ventricle eliminated the possibility of a ventricular septal defect. The wall of the infundibulum was 3 mm thick, while the wall of the right ventricle was 11 mm. thick The incision was closed with interrupted sutures Occlusion time was 5 minutes and 5 seconds Recovery was uneventful

Postoperative catheterization, on July 23, 1957, showed that the systolic pressure in both the right ventricle and the pulmonary artery was 26 mm Hg, there being no gradient whatsoever There was still no evidence of a shunt and peripheral arterial saturation was again normal Indicator dilution studies were normal.

The *electrocardiogram* showed only slight residual right ventricular hypertrophy When last seen, 8 months after operation, the patient was asymptomatic The thrill had disappeared, but a Grade 2 systolic murmur in the second left interspace remained It was concluded that the patient was cured (see Fig. 3).

CASE 4—D. S, a 20 year old white man, was first seen in May, 1954 He had been blue for 3 days after birth A heart murmur was noted. Growth was normal After the age of 10, he began to have syncopal attacks about every 6 months up to the age of 15, and more recently he had experienced mild exercise intolerance He was said to have had a dusky complexion, but no definite proof of cyanosis had been established

Physical examination of this well developed young man revealed slight duskiness of nail beds and lips, but no definite central cyanosis Prominent "a" waves were noted in the neck A slight right ventricular lift was present at lower left sternal border A systolic thrill and a harsh, Grade 4 systolic murmur were present over the precordium, maximal over the inner end of the second and third left intercostal spaces

The *electrocardiogram* suggested right ventricular hypertrophy

Fluoroscopy revealed enlargement of the right atrium and the right ventricle Prominent left but normal right and main pulmonary arteries were noted

Cardiac catheterization, on July 20, 1954, showed a gradient in systolic pressures of 75 mm Hg between main pulmonary artery and right ventricle, right ventricle, 100/-3 mm Hg and pulmonary artery, 19/6 However, this rise seemed to occur about one third of the way down the left border of the heart and not at the pulmonary valve level There was no evidence of a shunt and the systemic arterial O_2 saturation was normal The preoperative diagnosis was isolated infundibular pulmonic stenosis

Operation. On April 2, 1957, under general anesthesia, the patient was cooled to 30 5° C Bilateral thoracotomy, using the fourth intercostal space on the right and the third on the left side, was performed The heart was large, mainly on the right side, and the right ventricle was hypertrophied. A very small infundibular chamber, about 1 cm long, with a

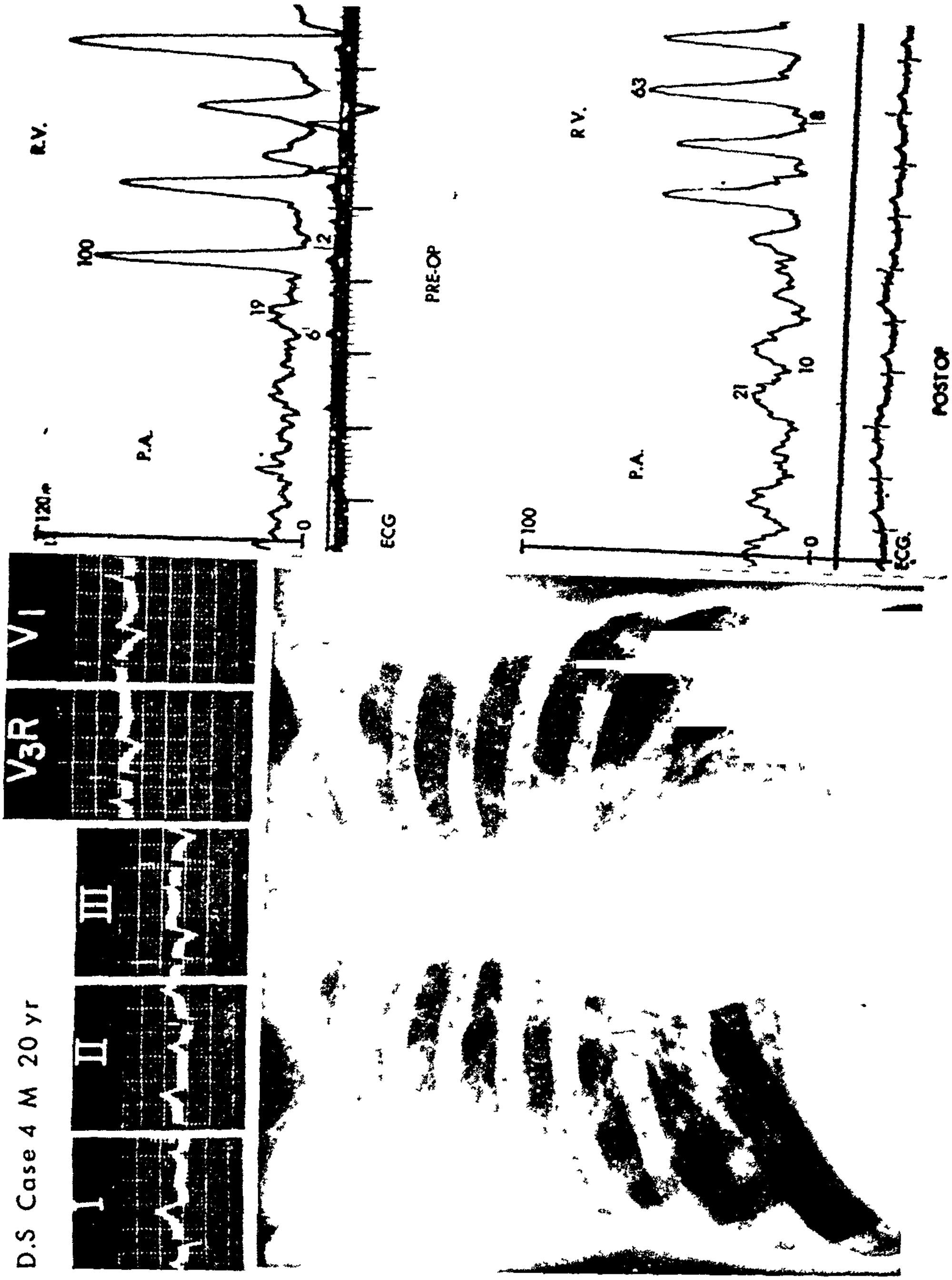

Fig 1.—Case 1 (D S), 20-year-old white man. Preoperative gradient of 81 mm Hg and postoperative gradient of 62 mm Hg.

thin wall, was seen The systolic thrill began in this chamber and was propagated on to the pulmonary artery where it was maximal over the mild post stenotic dilatation The outflow tract was infiltrated with 1 per cent procaine and, using inflow outflow occlusion and neostigmine bradycardia, an incision was made in the right ventricle extending up the outflow tract and into the small infundibular chamber. This involved cutting through a fibrous stenotic ring It was found that the infundibular chamber was triangular in section as the obstructing diaphragm ran upward and backward and almost fused with the pulmonary valve posteriorly. As much as possible of the obstructing sheet was excised. Palpation upward revealed a normal pulmonary valve and palpation downward revealed firm muscle around the finger in the outflow tract, but no actual stenosis. Closure was effected by a running suture in the incision Total occlusion time was 4½ minutes Recovery was uneventful

Postoperative catheterization, on May 16, 1957, 6 weeks after operation, showed a pressure of 63/8 in the right ventricle and a pressure of 21/10 in the pulmonary artery, and a systolic gradient of 42 mm Hg compared with 81 mm. Hg before operation An indicator dilution curve revealed no evidence of a right to left shunt

The *electrocardiogram* remained unchanged

Since operation he has had an increased exercise tolerance and has felt well There remains a Grade 2 systolic murmur of diminished intensity. The patient is clearly improved (see Fig 4)

CASE 5—L D, a 9½ year old white girl, was admitted in August, 1958 She had been known to have a heart murmur for 4 years prior to admission and had been having mild dyspnea on exertion and some fatigability. The previous winter she had had a severe upper respiratory tract infection

Physical examination revealed a right ventricular lift along the lower left sternal border A thrill and a harsh, Grade 4 systolic murmur were noted over the precordium, maximal in the second left intercostal space, but louder in the third than in the first space

The *electrocardiogram* showed right ventricular hypertrophy

Fluoroscopy revealed slight prominence of the main pulmonary artery and an enlarged right atrium and right ventricle

Cardiac catheterization, on Aug 15, 1958, showed a pulmonary artery pressure of 24/11 and a right ventricular pressure of 99/0 mm Hg The rise in pressure occurred low in the right ventricle There was no evidence of a shunt in either direction

The preoperative diagnosis was isolated infundibular pulmonic stenosis

Operation On Oct 27, 1958, under ether anesthesia, the patient was cooled to 30 5° C A large infundibular chamber with a thin wall was found while the main right ventricular wall was thick *The pulmonary artery was normal in size The thrill commenced at the lower* border of the infundibular chamber

On opening the chamber, it was found that the stenosis was formed by a muscular diaphragm with two small fibrous rimmed holes in it The pulmonary valve was normal The stenosis was excised by extensive dissection with knife and scissors After this procedure, the chordae tendineae of the tricuspid valve were easily seen No red blood entered the right ventricle The incision was closed by tying previously placed stay sutures Total occlusion time was 4 minutes, 50 seconds The thrill had now disappeared and the pulmonary artery was pulsating well

Postoperative catheterization, on March 20, 1959, showed that the pressure in the infundibular chamber was 20/0 mm. Hg and in the body of the right ventricle 30/0 mm Hg, thus, the systolic pressure gradient had fallen to 10 mm Hg (75 mm Hg before operation) (see Fig 5)

PATHOLOGY

It appears that infundibular stenosis is caused by arrest of the normal involution of the bulbus cordis which should be incorporated into the right

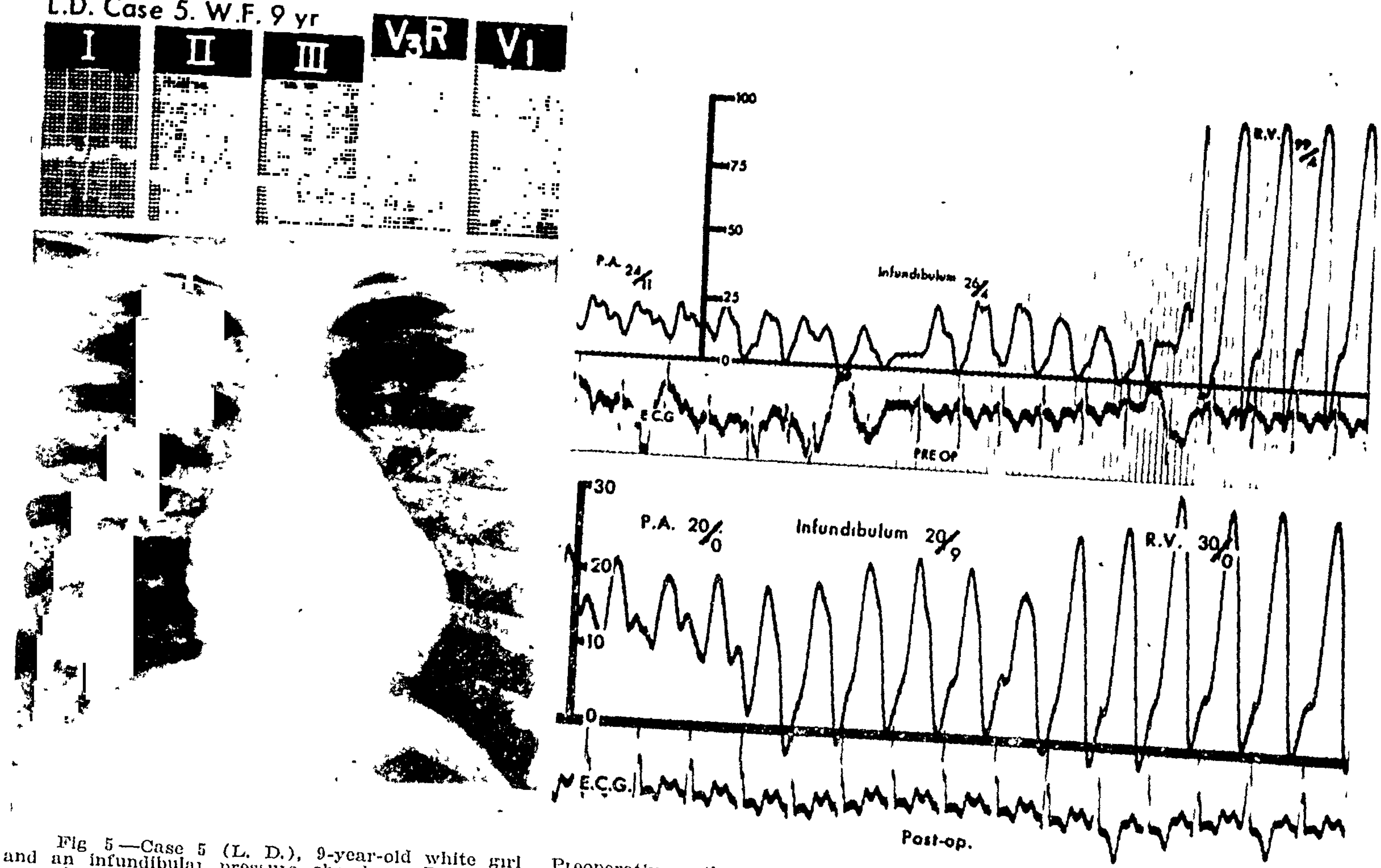

Fig 5.—Case 5 (L. D.), 9-year-old white girl. Preoperative catheterization showing systolic pressure gradient of 75 mm. Hg and an infundibular pressure chamber. Postoperative catheterization showing a gradient of 10 mm. Hg and an infundibular pressure chamber still present.

ventricle by the end of the second month of intrauterine life, thus forming the outflow tract of the right ventricle[6]

The stenosis, it is said, may be of two types (1) fibrous and muscular tissue create a narrowed area in some portion of the infundibulum dividing the right ventricle into two chambers of unequal size, the one with an hypertrophied wall, the other dilated and thin walled, and (2) the infundibulum is shrunken in size with thick muscular walls constituting a fusiform stenotic outlet extending over some distance[18] In our series, we have not encountered this latter type

CLINICAL DIAGNOSIS

History—A heart murmur may have been first noted at any age Such a murmur, of course, has really been present since birth The symptoms, if any, are identical with those of valvular pulmonic stenosis and include exertional dyspnea, fatigue, syncope, dizziness, anginal pain and, eventually, edema and right heart failure Clubbing and central cyanosis indicates the presence of a septal defect in both groups and rules out an isolated obstruction The history is of no aid in delineating the site of the stenosis

Physical Findings—The following points may help to differentiate infundibular stenosis from valvular stenosis (1) right ventricular precordial lift may be absent in very low infundibular stenosis, (2) the thrill and systolic murmur are usually maximal in the third left intercostal space in infundibular stenosis and higher up in valvular stenosis,[19] (3) the second heart sound may be widely split in infundibular stenosis with a normal or diminished pulmonary component, (4) usually no post-stenotic dilatation of the pulmonary artery is seen on x ray in infundibular stenosis and, in the right anterior oblique view, the left lower mid segment may bulge, and (5) on fluoroscopy, the pulsations of the main pulmonary artery are increased in valvular stenosis, but not in the infundibular type

Looking at our cases, the only one of the above features which occurred constantly was the lower site of the murmur and thrill These were always louder in the third than in the first space

Electrocardiogram—Right ventricular hypertrophy is present in both types of obstruction

Fluoroscopy—One would expect to note less post stenotic dilatation of the pulmonary artery with infundibular stenosis but, in our cases, we were unable to correlate the fluoroscopic findings with the actual anatomy seen at surgery in 2 of the 5 cases When the extremes (either very pronounced dilatation or apparent diminution in pulmonary artery size) are present, the finding is probably helpful, but in the intermediate stages, the fluoroscopy observations do not aid in the differential diagnosis

Thus, if our patients are representative, we find no important advance has been made in the clinical differentiation between isolated valvular and infundibular stenosis since Barie,[10] in 1895, noted that the murmur and thrill were located lower on the precordium in infundibular stenosis

Cardiac Catheterization.—It has been assumed that cardiac catheterization would be efficient in revealing three distinct pressure zones in pulling back from pulmonary artery to right ventricle, the lowest mean pressure being in the infundibulum.[11] In going from pulmonary artery through the valve into the infundibulum, the systolic pressure rises abruptly while the diastolic pressure remains constant. Moreover, the right ventricular pressure curve does not appear until the catheter tip is well below the valve level.

Despite this thesis, at times the diagnosis of infundibular stenosis comes as a surprise to the surgeon and the cardiologist at operation. Fabricius,[21] reporting on 50 patients submitted to pulmonary valvulotomy for either isolated pulmonary stenosis or the tetralogy of Fallot, had 5 cases in which catheterization was interpreted as revealing a valvular-type of stenosis yet, at operation, infundibular stenosis was present. Antonius,[22] in reporting 39 cases akin to those of Fabricius, found 11 cases of infundibular stenosis at operation of which only 2 were diagnosed by catheterization. This discrepancy has been commented upon by almost all groups with extensive experience in the surgery of pulmonic stenosis.

Kirklin[13] has stated that a sudden transition from pulmonary artery to ventricular pressure curve can occur not only in valvular stenosis but also in pure infundibular stenosis, if the obstruction is situated close to the valve. Certainly, this has been our own experience.

In 4 of our cases, the right ventricular pressure curve did not appear until the catheter was well below the usual site of the pulmonary valve. In the one exception, the site was not noted. We found this observation, when present, to be uniformly valid and we think that this is probably the best contribution of cardiac catheterization toward confirming the diagnosis of infundibular stenosis.

Other Methods of Diagnosis.—Rudhe[7, 23] and the group at the Karolinska Institute in Sweden describe selective angiocardiography and electrokymography as giving excellent results in differentiating valvular from infundibular stenosis. We have had no experience with these techniques.

Differential Diagnosis.—Besides valvular stenosis, the most difficult disease to differentiate from mild infundibular stenosis is the maladie de Roger. In mild infundibular stenosis the split of the second sound is wide and the thrill and murmur may be situated higher than in maladie de Roger. As the severity of the lesion increases, this differential diagnosis becomes much easier.[2]

Other entities that may simulate mild infundibular stenosis are atrial septal defect and mild aortic or subaortic stenosis. Careful clinical evaluation will avoid confusion with these entities. The differentiation between severe infundibular stenosis with patent foramen ovale and the tetralogy of Fallot, while very important, is not pertinent to this discussion of pulmonic stenosis with intact septa.

SURGICAL THERAPY

Like pulmonary valvular stenosis, the actual manipulative period of the excision of infundibular stenosis does not need to be very long, perhaps 4 to 6 minutes Therefore, the technique of hypothermia has proved quite safe and satisfactory for this procedure There appears to have been a widespread opinion that incision into the human ventricle is apt to precipitate ventricular fibrillation in the hypothermic patient This opinion was, no doubt, derived from animal experimentation, since, at 25° C, right ventricular incision in dogs invariably precipitates fibrillation This transference between species is merely another example of the danger of translating canine cardiac responses to man We have incised and later sutured the hypothermic right ventricular myocardium, after infiltration with 1 per cent procaine, in 16 patients whose rectal temperatures were between 26 and 31° C and have not seen a single episode of ventricular fibrillation as a result of this incision As in other operations suitable for hypothermia, accurate preoperative diagnosis relative to the integrity of the cardiac septa is important, lest the surgeon find himself at the operating table staring at an unexpected malformation, the correction of which would require cardiopulmonary bypass It is not critical, however, to distinguish infundibular from valvular stenosis since both are readily and safely treated using hypothermia alone

The transverse sternal splitting incision, utilizing the fourth interspace on the right and the third on the left, has proved ideal for both the vena cava dissections and the infundibular procedure A vertical sternal splitting procedure may be equally effective, provided that the skin incision is transverse and submammary to avoid the disfiguring scar usually left when the vertical sternal splitting incision is employed

Positioning of the patient so that the cardiotomy is as superior as possible is important to avoid trapping air, as it is in all other operations on the heart

After wide pericardiotomy to expose the myocardium, inspection of the right ventricle has immediately revealed the site of the pulmonic obstruction in all of our cases An infundibular chamber, whether small or large, has been seen, separated from the remainder of the hypertrophied tense ventricle by a distinct groove crossing the outflow tract The chamber bulges during early systole, thus having a paradoxical motion which puts it out of phase with the rest of the ventricle (One would suppose that this motion might be visible on occasion at the preoperative fluoroscopy) The vigorous systolic thrill invariably begins in the infundibular chamber, although in 1 patient with a very high obstruction (Case 4, D S), the thrill did not become maximal until the palpating finger was moved about 1 inch beyond the valve ring The pulmonary artery in this patient also showed slightly more post-stenotic dilatation than was seen in the other patients, although in none of them did this enlargement of the pulmonary artery approach that commonly seen with valvular disease

Tapes are placed around the two venae cavae near their entrance into the auricle We have routinely infiltrated the myocardium of the outflow tract above and below the infundibular groove with 1 per cent procaine to diminish the number of stimuli aroused by incision, retraction, and suturing of myocardium This step may not be necessary but, since no episodes of ventricular fibrillation have occurred, we have continued its use Stay sutures are placed to each side of the proposed incision, and one at each end, to aid in the rapid closure, which can be done while circulation is being restored

When all is ready, inflow occlusion is performed by traction on the tapes around the venae cavae. The aorta is cross-clamped about 1 inch above the heart and 1.0 to 1.5 ml. of 1:4,000 neostigmine is perfused into the coronary circulation by injection into the root of the aorta. The aortic clamp is then removed, and both aorta and pulmonary artery are clamped as close to the aortic roots as possible. This clamp is designed to stop coronary blood flow and to prevent back bleeding from pulmonary artery. The incision into the ventricle must then be made very rapidly so that distention of that structure will not occur.

The incision begins in the infundibular chamber when this structure is sufficiently large. It may traverse the stenosis or extend to a point just above it, as the occasion demands. Through this incision, the obstructing tissue is widely resected using whatever instruments the operator selects. Punches, scissors, and the knife may all be needed for a given situation. The extent of the resection should be as wide as is compatible with safety. The interventricular septum and the wall of the ventricle are, of course, preserved, but muscular bands involving the crista supraventricularis may be resected.

The failure of bright red blood to enter the right ventricle is taken as proof that no septal defect, however small, is present.

On conclusion of the definitive portion of the infundibular resection, the assistant pulls up on the stay sutures and the closure of the ventriculotomy by continuous suture is begun. At this point, blood is allowed to enter the right atrium and air is expelled from the heart via the incision. The clamp is then removed from the aorta and pulmonary artery so that blood flow to lungs and body is resumed. There may be some leakage of blood from the ventriculotomy during this period, but this is minimized by the assistant as the operator rapidly places the first layer of the continuous suture, thus sealing the incision. A second layer creating the so-called ''baseball stitch'' may now be placed leisurely, and reinforced with interrupted sutures as seems indicated. We have frequently reinforced this closure with a patch of pericardium sewn to the myocardium.

After the circulation seems satisfactory, the pericardium may be loosely closed, chest tubes placed, and the incision closed in the manner of the surgeon's choice.

RESULTS

Of the 5 patients, 2 had mild residual gradients, 1 had no gradient but a mild pulmonary hypertension (50 mm. Hg), while the other 2 had normal hemodynamics. All patients were much improved clinically, and it is felt that they now have cardiovascular physiology compatible with full exercise and long life.

SUMMARY

1. Of the 5 cases of isolated infundibular pulmonic stenosis presented, there was a correct diagnosis preoperatively in 4. The diagnostic criteria are discussed.

2 Operation was performed in each case during hypothermia, resecting the obstructing tissue under direct vision via a ventriculotomy

3 Hypothermia is ideally suited for the surgical treatment of isolated infundibular stenosis, since either valvular or infundibular obstruction can be effectively and safely treated using this technique alone

ADDENDUM

Since this report was made, 3 additional patients have been operated upon by the same method with excellent results

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DISCUSSION

DR. JOHANN L. EHRENHAFT, Iowa City, Iowa.—All of us who are doing open intracardiac surgery have and will encounter this relatively rare congenital anomaly under discussion. We have seen it in 5 patients. Being advocates of both methods, hypothermia and extracorporeal circulation, we have used the extracorporeal circuit in patients with infundibular muscular stenosis by preference, even though we prefer hypothermia for correction of pure valvular pulmonic stenosis. As it has been stated, the differential diagnosis between a valvular pulmonic stenosis and an infundibular muscular stenosis without an associated septal defect can at times be difficult. This is especially true if the muscular infundibular stenosis is located distal in the right ventricular outflow tract. The time required to completely resect this often massive muscular ridge is sometimes longer than one can gain by the use of hypothermia alone. This was brought home to us by a patient in whom we resected about 15 grams of right ventricular muscle before the right ventricular outflow tract obstruction was completely relieved and this required about 40 minutes.

If the infundibular muscular mass is completely resected, no residual thrill or murmur should exist and there should be no pressure differential between the right ventricle, the right ventricular outflow tract, and the pulmonary artery.

DR. GILBERT S. CAMPBELL, Oklahoma City, Okla.—A patient with isolated infundibular obstruction with an interesting antecedent history was recently admitted to the University of Oklahoma Hospital.

(Slide) I think the anatomy is depicted fairly well in this drawing by Dr. Richardson.

This next slide will show what was seen at the time of cardiotomy into the infundibular chamber.

This next slide will show a blow-up of the infundibular diaphragm.

This patient had a Brock procedure done in June of 1956, and the knife had been introduced and manipulated only in the infundibular chamber and the pulmonary artery. On re-admission in late March of this year the right ventricular systolic pressure was 164 mm. Hg. Following excision of this infundibular diaphragm, the systolic pressure in the right ventricle was 45 mm. Hg.

To date we have operated upon 11 patients at Oklahoma, and the defects include tetralogy of Fallot, partial A-V canal, atrial septal defect, infundibular stenosis (shown here), and isolated pulmonic stenosis. The mortality has been zero per cent.

DR. PAUL W. SANGER, Charlotte, N. C.—I would like to congratulate Dr. Hederman on his excellent English and his well-organized paper.

There is one thing I did not understand which I would like for him to explain. I thought he made the statement that with infundibular stenosis he also got post-stenotic dilatation, as we always get in valvular stenosis. This is a finding which has never been reported before and is against all hemodynamic principles as applied to post-stenotic dilatation. It has been an accepted diagnostic differentiating point that when post-stenotic dilatation occurred in the pulomary artery it was unquestionably always due to a valvular stenosis.

DR. FRANK GERBODE, San Francisco, Calif.—My ballot certainly is in favor of using extracorporeal circulation with most operations for relief of pulmonic stenosis, reserving hypothermia for the very young patients with valvular stenosis.

We have seen congenital infundibular stenosis in patients who have been very carefully screened and were thought to have pure valvular stenosis, and we have also found that there are not infrequently small interventricular defects associated with high infundibular stenoses.

Although it is possible, as has been shown by Henry Swan's very nice work, to resect the infundibulum utilizing hypothermia, my own belief is that extracorporeal circulation gives more security and the opportunity to perform a more complete operation.

In regard to Conrad Lam's paper, I am reminded of work we did in the experimental laboratory some years ago, when we, too, were studying hypothermia and pulmonic valve insufficiency. We wanted to resect the entire pulmonary valve I developed a very nice technique using hypothermia; then one day I came into the laboratory and found most of the dogs had already been done by one of the young men without the aid of hypothermia and with a lower mortality rate than when hypothermia was used This merely shows that one can usually do an open cutting procedure on the pulmonic valve without metabolic or circulatory support, but I certainly agree with Don Effler and some of the others that rapidity in this sort of thing is not always desirable Accuracy and the possibility of having to extend the operation make the use of extracorporeal circulation most desirable At the present time I do not believe that there is much inherent danger in using a properly designed and operated pump-oxygenator system.

DR HENRY SWAN, II, Denver, Colo —I would like to respond to Dr Gerbode by saying that we don't feel in any way that we are casting a vote at this time for any type of technique We use hypothermia; we use cardiopulmonary bypass We have happened to use a combination of both rather frequently We tend to use in our clinic the one which in our hands gives the best results to the patient at the lowest risk

The only real argument we have for using the open valvuloplasty and resection of the infundibulum using hypothermia is the very satisfactory end results achieved, Dr. Gerbode, as objectively measured in the vast majority of these patients, and the fact that in some 65 such patients there has not been a death. So we feel that this particular technique and this particular argument is pertinent to the use of the method

DR HEDERMAN (Closing) —First, I would like to thank the discussers for their suggestions

Two questions in particular I would like to reply to, one of Dr Sanger, who commented on the post stenotic dilatation. There was 1 patient who had very definite post stenotic dilatation, and this case was a boy who had an extremely high obstruction He had a very, very small triangular infundibular chamber, right up against the pulmonary valve, and the actual septum ran obliquely, so that posteriorly the septum was right up against the valve, and anteriorly there was only 1 cm distance between the valve ring and the lower edge of the infundibular chamber.

It is easy to see that in this instance the jet of blood coming through the infundibular stenosis, which was very tight in this case, would go right through the pulmonary valve and create the post stenotic dilatation in any of the ways that have been ascribed to be the cause of this condition

I think this case also emphasizes our statement that it is not always possible to diagnose this condition preoperatively Very careful cardiac catheterization will be needed in such cases as this, to differentiate either the infundibular chamber or the fact that the stenosis occurred a little below the valve It is interesting that this boy did show the lower site of murmur and thrill, which was described so many years ago by Barrie, and none of our more modern methods were effective So we feel that this is one of the reasons for doing these cases of pulmonary valvular stenosis under hypothermia rather than under normothermia, because it is possible, even with careful catheterization, to run into this kind of diagnostic difficulty with a very high infundibular stenosis I think Kirklin has also commented on this in a paper some years ago

Now the second question, if I am not running over my time. Dr Gerbode mentioned the I V. effect I should have added that in all our cases no red blood came into the right ventricle during the procedure

Finally, Dr De Bakey, I would like to thank the Association and members for this privilege of speaking on this side of the Atlantic to you all.

SURGICAL EXPERIENCES IN THE TREATMENT OF CONGENITAL MITRAL STENOSIS AND MITRAL INSUFFICIENCY

George W. B. Starkey, M.D., Boston, Mass.

CONGENITAL mitral valvular lesions are rare cardiac anomalies but can cause severe incapacitation and death in children. It would appear that some of these lesions are amenable to surgical therapy. At the Boston Children's Medical Center, 5 patients with severe congenital mitral stenosis and 2 with congenital mitral insufficiency have been operated upon between 1955 and 1958. The clinical, pathologic, surgical, and hemodynamic aspects of these cases will be discussed.

CONGENITAL MITRAL STENOSIS

Eleven cases of "pure" or uncomplicated congenital mitral stenosis were found in the literature. There were 38 additional cases but these were associated with other cardiovascular anomalies, usually left sided, such as, aortic stenosis, coarctation, patent ductus arteriosus, etc. Thirty-four of these cases were reviewed by Ferencz[1] and his associates and 9 new cases were added. Bower,[2] Maxwell and Young,[3] Kjellberg,[4] Braudo,[5] and Bernstein[6] and their co-workers have reported 7 further cases.

The prognosis in congenital mitral stenosis uncomplicated by other valvular or aortic lesions is poor, as pointed out by Braudo, since 8 of the 10 patients he reviewed were dead under the age of 2 years. Of the 5 in the literature who were operated upon only 2 were alive at the time they were reported, 1 for at least 7 months and another for 16 months.

Clinical Material.—

There were 5 patients with congenital mitral stenosis operated upon at the Boston Children's Medical Center. The age range was 2½ to 15 years. There were 3 girls and 2 boys. The diagnosis was made on the basis of the early age of detection of a mitral diastolic murmur (between the ages of 2 weeks and 14 months in 4 and at 5 years in the fifth patient). There was no history or other evidence of rheumatic fever.

All these children were very ill and in congestive failure. Severe respiratory infections, underdevelopment, and dyspnea were present in all. Three of

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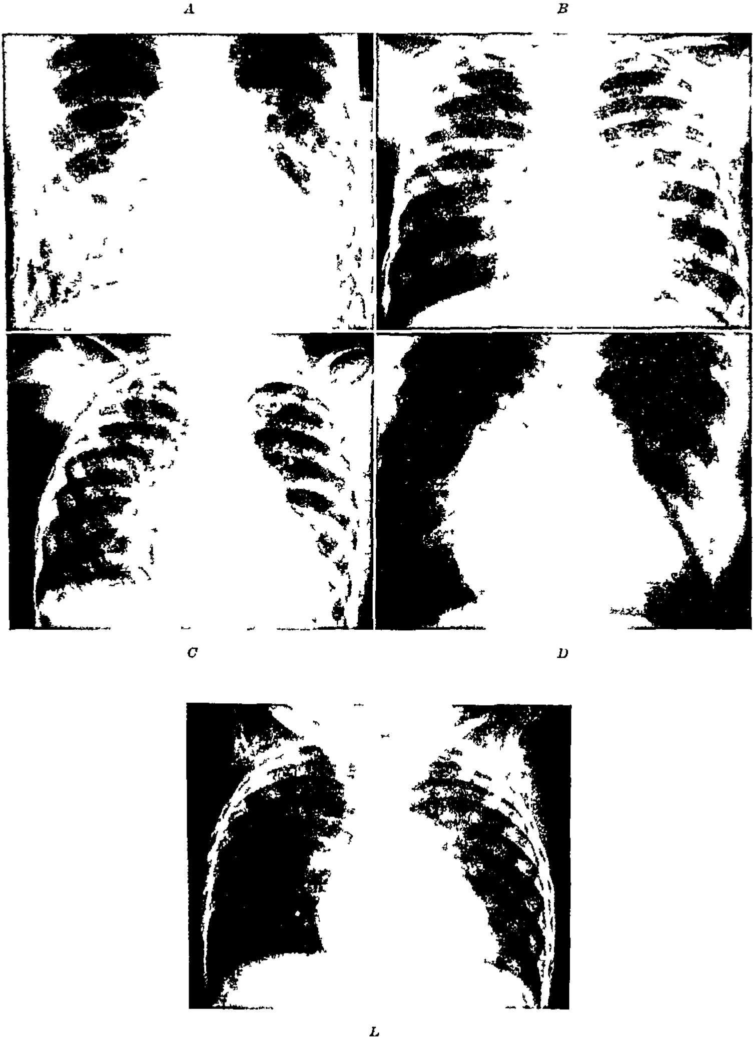

Fig 1.—Congenital mitral stenosis Preoperative roentgenograms A Case 1 B, Case 2 C, Case 3 D Case 4 and E Case 5

the 5 patients had had repeated bouts of syncope, often accompanied by cyanosis. A fourth patient had grand mal seizures accompanied by cyanosis during bouts of crying. Hepatomegaly was noted in all 5 patients, splenomegaly in 3. The cardiac findings revealed normal sinus rhythm, an apical diastolic rumbling murmur, loud P_2, P pulmonale in all 5 patients. An apical systolic blowing murmur was found in 3 and right ventricular hypertrophy in 4. By x-ray examination there was cardiomegaly in all, with enlargement of the right ventricle, left atrium, and pulmonary artery (Fig. 1).

Four patients were catheterized preoperatively. There was evidence of marked elevation in pulmonary capillary pressure (27 to 30 mm. Hg mean), reflecting obstruction at the left atrial level. There was also increased pulmonary vascular resistance from 4.0 to 10 units (normal 3 units). In 2 patients studied postoperatively, 1 showed reduction in pulmonary artery pressure and both showed reduction in pulmonary capillary pressures.

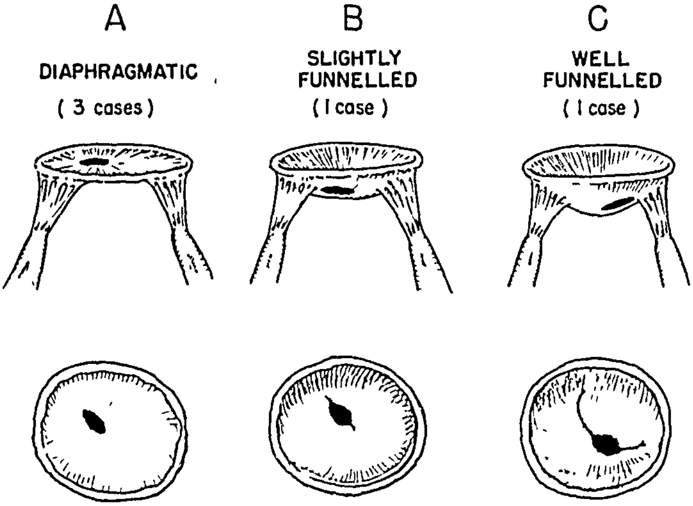

Fig. 2.—Congenital mitral stenosis. Schematic representation of valve types encountered at the time of surgery.

Surgical and Pathologic Considerations.—

Four of these patients were operated upon by the "closed" method using a standard left fourth intercostal space incision. There was one death on the fifth postoperative day for reasons that were not clear. Actually this patient had been doing quite well but died very suddenly after a meal, accompanied possibly by aspiration of food. No postmortem was obtained. A fifth patient was operated upon by the "open" method using a pump-oxygenator. At the end of the procedure the heart began to fail and could not be resuscitated.

All five patients had very large left atria. The junction of the appendage with the left atrium was small in most of these children, allowing entry only of the operator's fifth finger. There was no evidence of cor triatriatum. This was established by feeling both the mitral valve and at least one pulmonary vein orifice communicating with the single left atrial chamber approached by the appendage. Three of the valves were quite flat, thickened, and diaphragmatic with either no or poorly defined commissures (Fig 2). All three of these required incision with a guillotine knife. The fourth valve was well funnelled and had quite well-defined commissures This valve was opened with the finger alone. The fifth patient operated upon with the aid of the pump-oxygenator had a funnelled valve, but thickened leaflets with practically no commissural definition This valve also required incision In all cases there was shortening and some fusion of the chordae tendineae. The atrial appendages all showed endocardial sclerosis and no evidence of rheumatic fever. Two lung biopsies showed pulmonary vascular changes compatible with those described by Parker and Weiss[7] There was no calcification of the mitral valves and no left atrial thrombi.

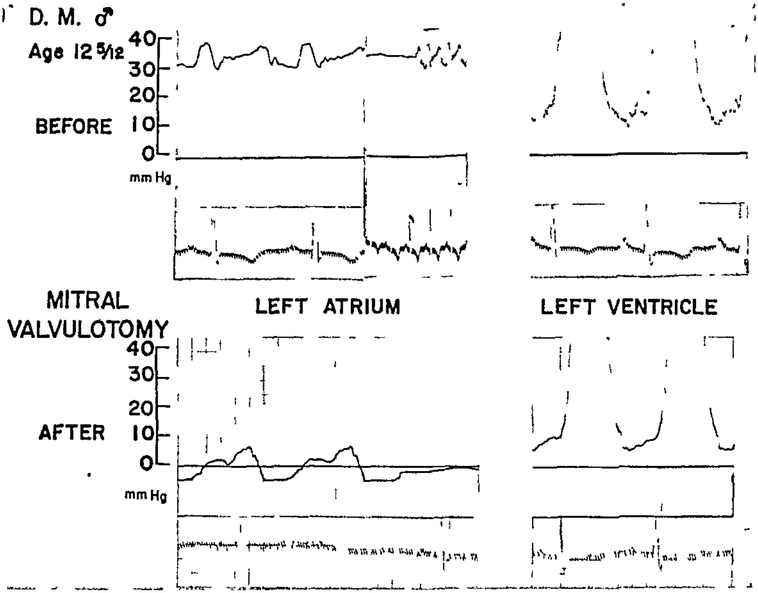

Fig. 3 —Congenital mitral stenosis (Case 1, D M) Direct readings at operation showed a left atrial—left ventricular gradient of 23 mm Hg There was no gradient post-commissurotomy.

Case Presentations.—

Case 1 —D. M. was a 12 year old white boy in whom a mitral diastolic murmur was first heard at the age of 2 months. His early years were characterized by limited activity and frequent respiratory infections In the few years before operation he was tutored at home and had a progressively downhill course. He had had twenty five hospital admissions for respiratory infections and congestive heart failure.

On admission to the Children's Medical Center, he had a respiratory infection and heart failure; present also were cardiomegaly, hepatomegaly, and clinical signs of severe mitral stenosis. He was placed in oxygen and treated medically very vigorously with diuretics, digitalis, antibiotics, etc. A right heart catheterization revealed an elevated pulmonary artery pressure (mean, 75 to 95 mm. Hg). Unfortunately a good pulmonary capillary pressure was not obtained. An attempt at left heart catheterization was contemplated but a small amount of general anesthesia dropped the blood pressure below 70 mm. Hg so that the plan was abandoned.

On Dec. 2, 1955, a mitral commissurotomy was done in the usual manner through a left fourth intercostal space incision. The pulmonary artery was large and turgid. Direct pressure readings revealed a PA pressure of 145 mm. Hg, left atrium pressure of 35 mm. Hg (mean), and left ventricular diastolic pressure of 12 mm. Hg (mean). This boy had a well-funnelled valve with a posterior opening not greater than 3 to 4 mm. in size. The commissures were quite well developed with thickening and fusion along the edges. The leaflets were quite supple. The valve was opened up to 2.5 cm. digitally and some anterior subvalvular stenosis also relieved. No obvious regurgitation was noted before or after the commissurotomy. No gradient could be demonstrated post-commissurotomy across the mitral valve, whereas there had been a 23 mm. Hg mean gradient before commissurotomy (Fig. 3).

This boy has been converted from a very restricted life in which even a few steps would cause dyspnea to one in which he goes to school, climbs stairs, walks a mile or two, and engages in mild athletic activities. Preoperatively he was hospitalized twenty-five times for heart failure and respiratory infections, and, in over 3 years since operation, he has not been hospitalized for these complaints.

CASE 2.—M. R. was a 6-year-old boy in whom a mitral diastolic murmur was discovered during a preschool physical examination. In the last year he had been somewhat restricted in activity and was tutored at home. He had had two or three bouts of dyspnea, cyanosis, and collapse often associated with anterior chest and upper abdominal pain. During his hospital stay he had numerous bouts of pulmonary edema and was very difficult to control on digitalis, diuretics, and salt restriction. The diagnosis of severe congenital mitral stenosis was made. Because of his precarious condition, a catheterization was not done preoperatively —the only patient of the 5 who did not have a preoperative study.

On Sept. 24, 1956, a mitral commissurotomy was performed, using a left fourth intercostal space approach. There was a 25 mm. Hg diastolic gradient at operation before enlarging the valve orifice and a residual 18 mm. gradient at completion of the operation. The valve was flat, thickened, and diaphragmatic. The opening was enlarged from 0.5 cm. to 1.5 cm. with the use of a guillotine knife. No commissures could be felt. There was shortening and thickening of the chordae tendineae. Since some regurgitation was being created, it was thought advisable not to enlarge the opening further.

This patient did well postoperatively and now goes to school. His activity has been much increased but he obviously now has some mitral regurgitation which limits him somewhat.

CASE 3.—S. H. was a 3½-year-old Negro girl who was a premature baby weighing four and one-half pounds. A mitral diastolic murmur was first heard at 3 weeks of age. During her first 2 to 3 years of life, this patient had repeated respiratory infections with questionable heart failure which required antibiotics and oxygen. At 3 years of age, she was digitalized. On admission to the hospital she appeared to be underdeveloped and chronically ill. She had both mitral diastolic and systolic murmurs at the apex; there was also hepatosplenomegaly. Right heart catheterization revealed a mean pulmonary artery pressure of 80 mm. Hg, a mean pulmonary capillary pressure of 29 mm. Hg, and a pulmonary vascular resistance of 9 to 10 units (normal up to 3 units). An electrocardiogram revealed right ventricular hypertrophy.

On Nov. 8, 1957, a mitral commissurotomy was performed through a left fourth intercostal space incision. The valve was diaphragmatic, thickened, and only slightly funnelled, with no obvious commissures. The opening was only 2 to 3 mm. in size and situated very close to the mitral ring The valve was opened with great difficulty, using the fifth finger, guillotine, and mitral dilators. Since some regurgitation was being produced, the valve was only opened to 7 to 8 mm One had the impression that there was a mass of fused chordae tendineae beneath this opening.

This patient did reasonably well for 5 days postoperatively but suddenly died after finishing lunch. No postmortem examination was done It was thought that aspiration of some food had occurred

CASE 4—J. K was a 15 year old white girl in whom a mitral diastolic murmur was first heard at the age of 9 months Until the age of 13 years she had led a rather restricted life because of dyspnea, but at that time she had a spinal fusion performed for severe congenital lumbodorsal scoliosis At the time of this operation she developed pulmonary edema Because of her incapacity she was tutored at home. At the age of 15 years, a right heart catheterization showed a pulmonary artery mean pressure of 65 mm Hg, a pulmonary capillary mean pressure of 27 mm Hg, and a pulmonary vascular resistance of 9 0 units. Pulmonary function studies showed a restrictive deficit of 50 per cent Because of her scoliosis no left heart catheterization was done It was thought that the mitral stenosis was severe enough to warrant operation She had no evidence of rheumatic fever in the past

On Nov. 20, 1957, a mitral commissurotomy was performed through a left fourth intercostal space incision The valve was diaphragmatic with firm thickened leaflets There was a posteriorly placed 4 mm opening and minimal evidence of commissure formation There was no calcification or thrombus The opening was enlarged digitally (fifth finger) up to 1 cm but, because of the firm rubbery consistency, a guillotine knife was used to increase the opening to 2 cm There was no obvious regurgitation before or after surgery but there was some fear that it might become a problem if any more enlargement of the orifice was undertaken A diastolic gradient of 24 mm Hg was measured across the mitral valve before the commissurotomy and an 8 mm Hg gradient noted afterward These were pressures taken at the time of surgery.

This patient did quite well immediately postoperatively. She eventually went to school rather than being tutored at home and was, in general, more active She still is restricted and has some trouble from respiratory infections but seems to be better than preoperatively It has been difficult to separate her cardiac from her pulmonary functional deficiency

CASE 5—F B was a 2½ year old white boy who weighed five pounds and four ounces at birth From the age of 2 months he had had repeated bouts of dyspnea and cyanosis with congestive heart failure which required six hospital admissions A mitral diastolic murmur was heard at about 14 months of age and was accompanied by a mitral systolic murmur On his last admission, at the age of 2½ years, he was in congestive failure with hepatomegaly, and right ventricular hypertrophy as disclosed by electrocardiogram and x ray studies A right heart catheterization revealed a pulmonary artery mean pressure of 45 mm Hg and a left atrial pressure of 30 mm Hg (catheter passed into left atrium via a small patent foramen ovale). His pulmonary vascular resistance was 4 units

On Dec 13, 1957, this patient was operated upon by way of a bilateral transsternal thoracotomy The patient was attached to a pump oxygenator The heart was stopped with potassium citrate and the left atrium explored via the right atrium and interatrial septal approach The mitral valve was somewhat funnel shaped with a centrally placed 5 mm opening There was some commissural definition The valve was opened with scissors, anteriorly and posteriorly, up to 1 5 to 2 cm The chordae tendineae were thickened, shortened, and fused It was difficult to be sure just where the incisions should be made because of the subvalvular fusion and poor commissure formation The left ventricle and atrium were filled with saline and the interatrial septum incision closed The right atrium was closed and the aortic clamp released The heart action returned but it was quite ineffective and, in spite of all efforts to resuscitate it, the heart finally stopped

A postmortem examination revealed thickening of the left atrial endocardium, fusion and shortening of the chordae tendineae and papillary muscles There was hypoplasia of the left ventricle with some left ventricular outflow obstruction proximal to the aortic valve. The exact cause of death was not clear but it was thought that the additional load on the hypoplastic left ventricle might have been a factor.

CONGENITAL MITRAL INSUFFICIENCY

Two patients with congenital mitral insufficiency were operated upon within the last year. Neither of these patients represented the more common types of

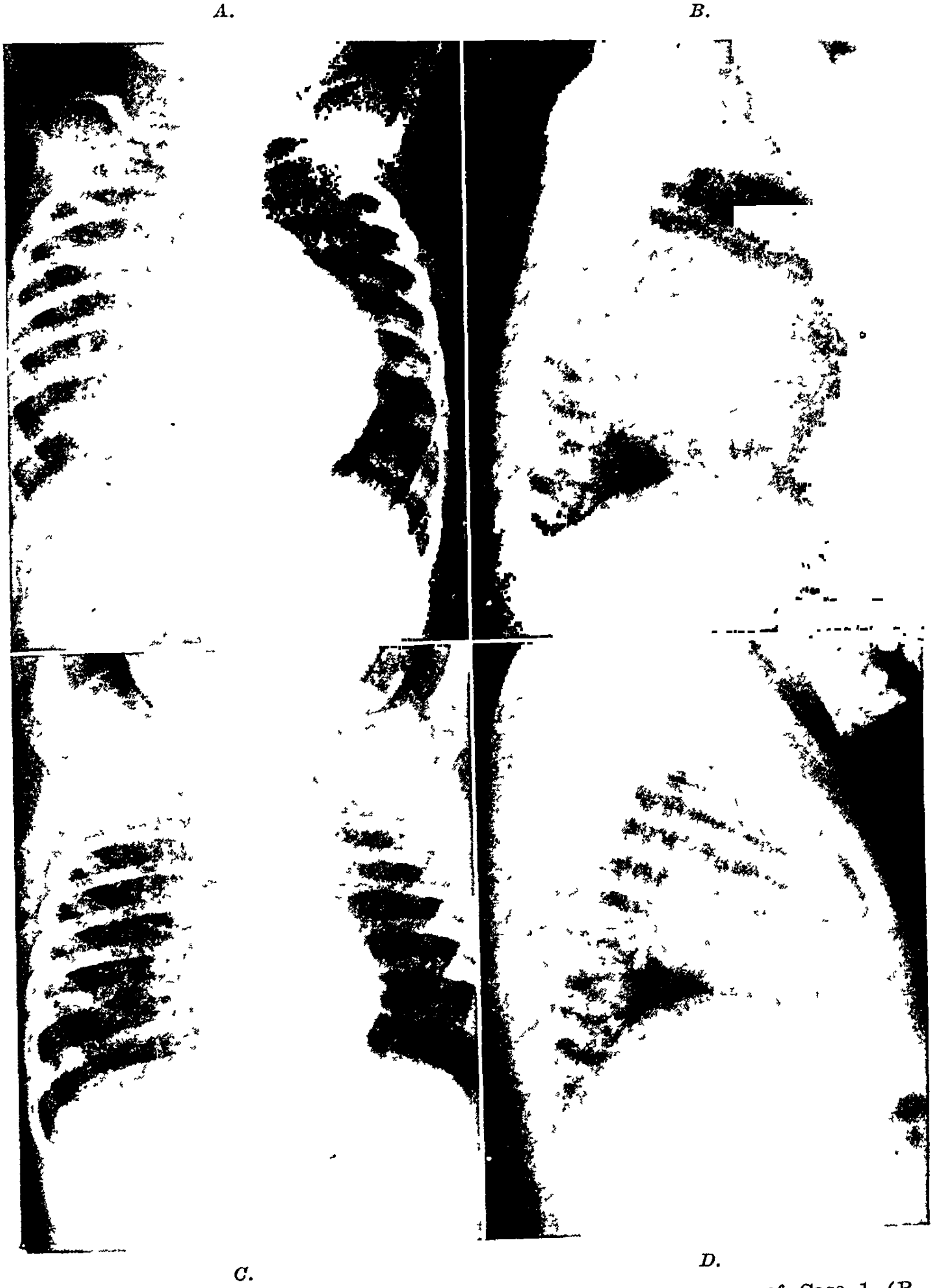

Fig. 4—Preoperative (A, B) and postoperative (C, D) roentgenograms of Case 1 (P. B.). This patient had congenital mitral insufficiency.

congenital mitral regurgitation; that is, a cleft mitral septal leaflet associated with an ostium primum or atrioventricular canal, or the rarer absent or vestigial posterolateral mitral leaflet.[8] These 2 children, like the 5 previously described cases of congenital mitral stenosis, were very ill and doing poorly on a strictly supervised medical program. One of these patients was operated upon using an "open" method with the aid of a pump-oxygenator, followed by some improvement, and the second was operated upon using a "closed" method with an excellent result.

A brief summary will best bring out the salient features of these 2 unusual cases.

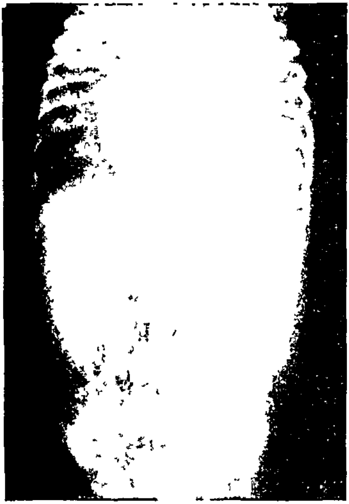

Fig 5.—Congenital mitral insufficiency (Case 1 P B) Angiocardiogram from left femoral vein showing large pulmonary artery with no left branches, and a large left atrium

Case Presentations.—

Case 1.—P. B was a 15 month old, eighteen pound, white boy admitted with cough, fever, cyanosis, and dyspnea. He had entered the hospital 4 months previously for investigation of his cough and dyspnea which were associated with mitral systolic and diastolic murmurs and a large left atrium An attempt at right heart catheterization at this time was unsuccessful because of the onset of auricular flutter. On re entry in July, 1958, he had a hacking cough, temperature of 102° F, pulse of 140, and a respiratory rate of 50. He was pale and cyanotic. He had an enlarged heart (Fig 4), mostly left atrium, and a Grade 3 mitral systolic murmur with a questionable short diastolic rumble Breath sounds were diminished on the left with hyperresonance on that side The liver was down 4 cm The patient was put on digitalis, oxygen, low salt intake, and antibiotics. He improved and was discharged only to return in August, 1958, at which time he was again cyanotic and pale, febrile, and in heart failure. He was treated vigorously, and again an attempt at right heart catheterization made The mean pulmonary arte [illegible] was [illegible]

Hg, pulmonary capillary pressure 22 mm. Hg (mean), and femoral artery pressure 95/47 mm. Hg (mean, 62 mm. Hg). The femoral artery oxygen saturation was 60 per cent, but with oxygen rose to 95 per cent. No shunt was demonstrated. An angiocardiogram (Fig. 5) showed a large pulmonary artery with a right branch but essentially no left branch. It also demonstrated a very large left atrium. The chest films over a period of several weeks had shown progressive diminution in the left pulmonary vascular markings accompanied by overdistention of the left lung. Eventually, the patient developed atelectasis, pneumonia, and fluid on the left side. The progressive loss of pulmonary vascular markings and subsequent atelectasis of the left lung were thought due to compression by the giant left atrium. Rivkin,[9] Murphy[10] and their associates have described this in the past. The diagnosis of congenital mitral insufficiency, possibly associated with some stenosis, was made. The posibility of a left atrial tumor or cor triatriatum was not ruled out but, because of the progressive downhill course of this child, he was taken to the operating room from the catheterization laboratory. He had a temperature of 103° F., pulse over 140, and atelectasis of the left lung the day of the operation. The white cell count was 27,000.

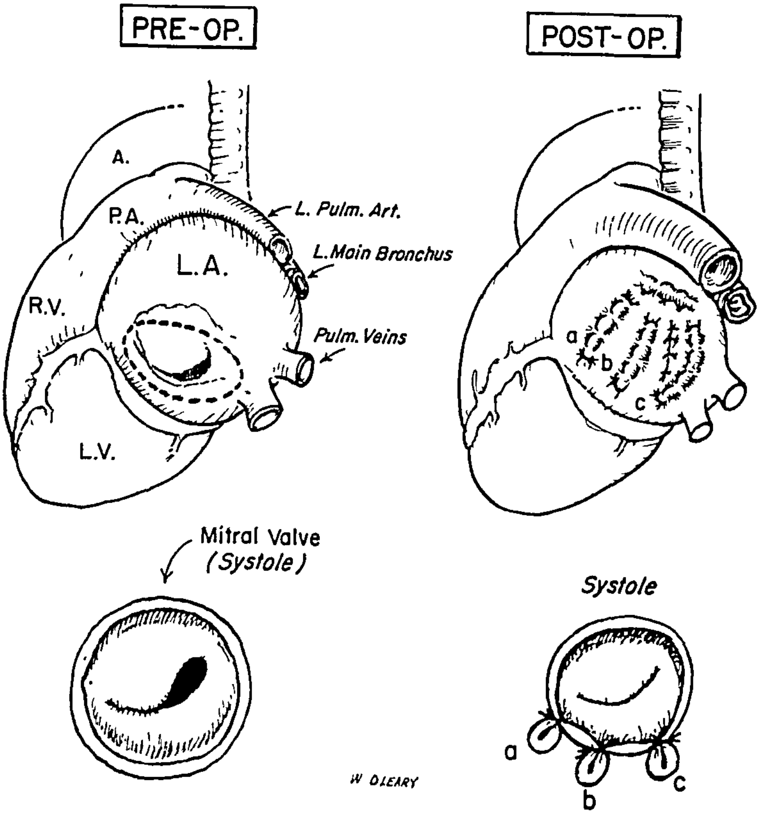

Fig. 6.—Repair of congenital mitral regurgitation. Preoperative view showing enlarged left atrium compressing left main pulmonary artery and bronchus. Postoperative view showing left atrium smaller and no compression of left main pulmonary artery and bronchus. Mitral ring sutures *a*, *b*, *c*, have now made the mitral valve competent.

On Aug. 29, 1958, the patient was explored through a left fourth intercostal space incision. There was a considerable amount of clear yellow fluid in the left pleural space. The left upper lobe was atelectatic and pneumonic. The left lower lobe was almost totally collapsed. The heart was very large. The pericardium was opened and a moderate amount of fluid removed. The striking thing about the heart was the giant left atrium which was compressing the left main bronchus and pulmonary artery. On depressing the upper surface of the left atrium, the lower lobe immediately re-expanded and the left main pulmonary artery distended There was a readily palpable systolic thrill over the left atrium, particularly posteriorly and superiorly There was a barely palpable diastolic thrill over the left ventricle. The main pulmonary artery was large and turgid Both the right and left ventricles seemed hypertrophied.

The left atrium was entered through a large appendage There was no tumor and no evidence of cor triatriatum There was a very forceful systolic jet coming from a posteriorly situated, 1 cm, mitral valve opening The mitral valve had a poorly formed anterior commissure and the valve itself was quite flat and taut, the valve ring seemed quite enlarged The valve was opened up to 1 5 cm and then 2 0 arterial sutures on large round needles placed through the left atrial wall and ring, guided by the intra atrial finger The needle was then guided out through the atrial wall and the suture tied This seemed to make the ring smaller and so three or four such sutures were carefully placed near the left circumflex coronary artery and great cardiac vein In this way several tucks were taken in the mitral ring posteriorly, laterally, and anteriorly The systolic jet seemed to disappear The sides of the tremendous left atrium were then reefed up as illustrated (Fig 6) to make the left atrium smaller and thereby take the pressure off the left pulmonary artery and bronchus The left lower lobe expanded well but the left upper lobe remained airless Because it was a solid pneumonic lobe and a possible source of difficulty, it was quickly removed

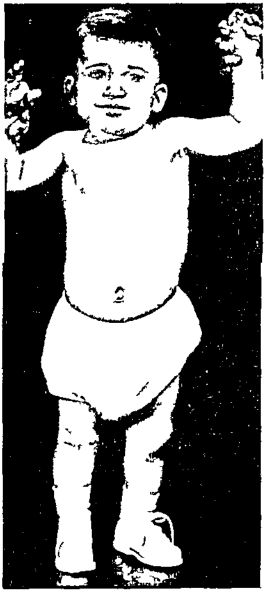

Fig 7 —Congenital mitral insufficiency (Case 1, P B) Photograph made 8 months postoperatively

The patient did very well postoperatively and left the hospital on the eighth day following surgery—afebrile, acyanotic, off antibiotics, and with a normal white count. He has remained on digitalis The left atrial appendage showed endocardial sclerosis and the left upper lobe demonstrated a chronic pneumonia but with pulmonary vascular [illegible] compatible with the Parker Weiss syndrome.

This boy was seen in April, 1959 (Fig. 7), 8 months postoperatively. He seemed perfectly healthy with a clear chest, normal-sized heart (see Fig. 4) and with Grade 1 mitral systolic and diastolic murmurs. He walks and runs, eats well, and weighs twenty-eight pounds, in contrast to his eighteen pounds at the time of operation. He has had no respiratory infections or difficulty since operation.

Case 2.—R. F. was an 11-year-old white boy with a known mitral systolic murmur since the age of 9 months which was associated with cardiomegaly. For the past several years he had had many bouts of dyspnea, weakness, and occasional cyanosis. He also had many epistaxes but no local or systemic cause could be found. In June, 1958, he was admitted to the hospital in congestive heart failure. At this time he was digitalized and put on Diuril and a low sodium diet. He improved somewhat and was discharged. He returned again in September, 1958, having been markedly restricted in his activities. At this time he was leading a bed-to-wheelchair existence with minimal walking because of fatigue and dyspnea. It was thought at this time that he had dominant mitral insufficiency and some aortic and tricuspid insufficiency. He had no evidence of rheumatic fever at any time.

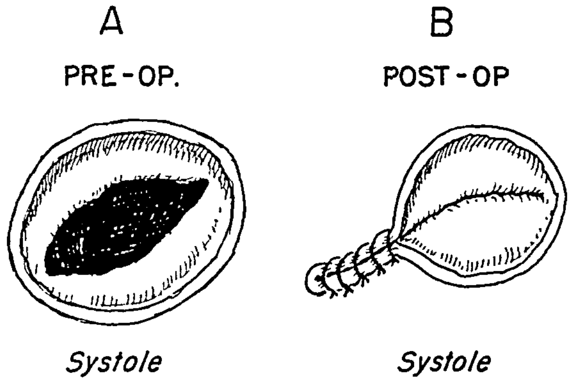

Fig. 8.—Surgical relief of congenital mitral insufficiency due to enlarged mitral ring (Case 2, R. F.). *A*, Preoperative view of valve in systole. *B*, Postoperative view of valve in systole, showing sutures in mitral ring over the posteromedial commissure.

A right heart catheterization revealed a low cardiac output, a pulmonary artery mean pressure of 47 mm. Hg, a pulmonary capillary mean pressure of 25 mm. Hg, and an aortic pressure of 88/65. There was also some suggestion of tricuspid regurgitation. The electrocardiogram showed left ventricular hypertrophy.

On Oct. 9, 1958, he was explored through a right fourth intercostal space incision. The heart was enlarged, particularly the left ventricle and left atrium. There was a systolic thrill over the left atrium and a lesser one over the right atrium. The patient was then attached to the pump-oxygenator after cannulation of the venae cavae and right subclavian artery. Just as the cannulation was being completed, the heart stopped but responded to intermittent compression and improved once the perfusion began. It was apparent that the left atrium remained full of blood and that the systolic jet, though less, was still palpable in the left atrium. A small incision was made into the left atrium, anterior to the right pulmonary veins, and a sucker inserted. It was obvious that the left atrium was being rapidly filled from the left ventricle due to the aortic regurgitation. Because of this, the ascending aorta was clamped above the coronary arteries and the left atrium then collapsed and became dry. The heart was then stopped and the left atrium opened widely. The mitral ring was very large. There was no slit in either leaflet of the mitral valve, nor was there any rupture of the chordae tendineae. The leaflets were somewhat thickened and very pale, suggesting endocardial sclerosis. The enlarged ring was therefore made smaller by inserting six 2-0 arterial sutures into the ring on either side of the posterior commissure (Fig. 8). These were then tied until the leaflets seemed to approximate each other. The orifice was diminished from at least three fingers to just a bit less than two fingers. This procedure seemed to make the rather flattened valve more funnel shaped. The somewhat thickened and taut chordae tendineae were also more relaxed. The left side of the heart was then allowed to fill with blood and the atriotomy closed. The aortic clamp was released and the heart started sluggishly but soon resumed a normal sinus rhythm. The systolic thrill was not palpable over the left atrium at a systemic blood pressure of 85/68. The right atrial systolic thrill remained about the same. Because of the long procedure and precarious condition of the patient, no direct investigation of the aortic or tricuspid valves was attempted.

The patient's early postoperative course was stormy but he eventually improved and was discharged—15 days after his operation. Follow up visits have shown some diminution in the heart size (Fig. 9), particularly of the left atrium. Both the patient and his parents feel that his exercise tolerance has improved. He still has an aortic diastolic murmur and some mitral insufficiency by auscultation. Six months postoperatively he is able to go up a flight of stairs, sleeps flat, plays basketball, and rides a bicycle. He could do none of these things preoperatively.

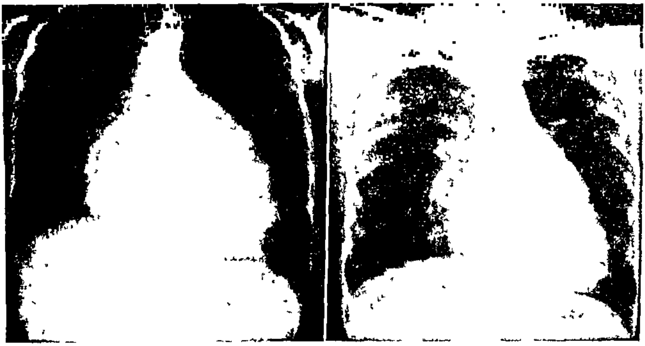

Fig 9—Congenital mitral insufficiency (Case 2, R. F) *A*, preoperative roentgenogram which shows large left ventricle, left atrium, and pulmonary arteries *B*, Postoperative roentgenogram (6 months) which shows diminution in size of left ventricle, left atrium, and pulmonary arteries.

DISCUSSION

Congenital mitral stenosis is a rare cardiac anomaly and carries a grave prognosis. It is not too difficult to recognize by simple clinical and laboratory methods. It is characterized by the early onset of a mitral diastolic murmur and evidence of pulmonary arterial and left atrial hypertension. Pathologically there appears to be a broad spectrum of findings beginning on the one extreme with a flat, thickened, diaphragmatic valve with little or no commissural formation, with short fused chordae tendineae, to the other extreme where one finds a well-funnelled valve with fused, well-formed commissures and fairly supple leaflets. The degree of endocardial sclerosis or subendocardial fibroelastosis seems greater in the first-described or more primitive-type valve and less pronounced in the more nearly normal-appearing valve. Since the prognosis is so poor in this condition, it would appear that surgery should be given a fair trial. Whether an "open" or a "closed" method should be used still remains unsettled.

Congenital mitral regurgitation not associated with an ostium primum defect or atrioventricular canal defect appears to be an even rarer lesion. In these 2 reported cases, dilatation of the mitral ring was the dominant feature. An "open" method of surgical approach would seem to give greater latitude in the type of repair for this defect.

SUMMARY

Five cases of congenital mitral stenosis treated surgically are reported. The clinical, pathologic, hemodynamic, and surgical aspects of the problem are discussed. There were four "closed" type operations with one death. In the 3 survivors, there was one excellent result and two fair to good results. A fifth patient was operated upon with the use of a pump-oxygenator but died at the end of the procedure.

Two patients with congenital mitral insufficiency were operated upon with no deaths. One had an excellent result and one a good result.

These two congenital mitral valve anomalies appear to be rare and carry a very poor prognosis. It is suggested that this diagnosis be more seriously entertained in the future and that surgical intervention be undertaken in these seriously ill children.

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DISCUSSION

DR. WILLIAM H. MULLER, JR., Charlottesville, Va.—Congenital mitral stenosis is indeed a relatively rare malformation which presents a real problem when it is encountered. I am very pleased to have had an opportunity to hear Dr. Starkey's interesting presentation this morning.

When we have operated upon patients with congenital mitral stenosis, using a closed method, mitral insufficiency invariably resulted The first patient on whom we performed an open operation, utilizing the pump oxygenator, had a diagnosis of corrected transposition of the aorta and pulmonary artery and congenital mitral stenosis We found a situation similar to that which Dr Starkey described, that is, a narrowed valve in which no commissural fusion lines could be seen Incisions were made in the valve approximately where we thought the commissures should be This child likewise did not survive the procedure More recently, however, we have operated upon a patient in whom Dr. Frank Dammann made a diagnosis of isolated mitral stenosis We found, just as Dr Starkey did, that there was thickening of the valve and shortening and fusion of the chordae tendineae Incisions were therefore made into the valve *leaflets* opposite *the* chordae attachments and the *papillary* muscles were split down to their bases The incisions were made actually into the anterior leaflet of the mitral valve

One can make three incisions we made only two in this patient, but obtained what we thought was a normal sized mitral valve This patient had no resultant mitral insufficiency, and has made an uneventful recovery and is greatly improved We think therefore that the incisions should be made through the valve leaflet, chordae tendineae and papillary muscles rather than where one thinks the commissures should be in this type of mitral stenosis.

DR. GEORGE A CLOWES, JR, Cleveland, Ohio —I, too, greatly enjoyed Dr Starkey's excellent presentation.

I would like to say a word about the matter of the approach to the mitral valve by open surgery Before at these meetings we have heard remarks by Dr Lillehei, Dr Kay, and others All of these authors have recommended the right sided approach to the mitral valve for open surgery I would just like to give you a little of our experience in approaching it from the left side

(Slide) This is done by cannulating externally, as you see here, the inferior vena cava through the saphenous orifices into the femoral veins and inferior vena cava, through the internal jugular vein and down into the right heart A ligature is placed around the pulmonary artery excluding the left side from the circulation. Perfusion is continued through the femoral artery

We have had experience with 8 cases in this fashion Most of them have been mitral insufficiency We have had one death and four very satisfactory results That is not the point The thing is that the left sided approach does, in my opinion and in the opinion of those of us who have worked with it, have some advantages

First of all, with the patient tipped 'way up on his right side, almost over toward the face down position, the mitral valve becomes the highest point in the ventricle, and therefore any air that is trapped is expelled through it rather than into the aorta, avoiding an embolus There is one point I would make before leaving this slide That is, one must thread this catheter down into the right ventricle before occluding the pulmonary artery, to avoid distention of this chamber, otherwise failure will result This was the cause of the death I mentioned

This slide shows the exposure of the mitral valve that was obtained in a 14 year old girl through the left sided approach In our experience this is much easier than the approach through the right side, in that the valve is much closer to one and easier to work on.

This slide shows the valve of another patient who was operated on by this technique, a 53 year old woman

This slide shows her appearance postoperatively I think we will leave the rest out

Dr Cross, last year at this meeting, described his experiences with operating on dogs in the right and left sided approach He stated that from the right side he had less air embolus Our experience has been different from this We find that this matter of placing the mitral valve highest in the heart is of some importance in this regard

Thank you very much I take this opportunity again to say how much I have enjoyed Dr Starkey's nice presentation, and hope that perhaps this technique may be of some use to some of you

DR. CHARLES P. BAILEY, Philadelphia, Pa.—I very much enjoyed this talk of Dr. Starkey's because we have had a somewhat similar experience.

Actually, I have operated on only 4 children with congenital mitral stenosis. The pathology is distinctly different, of course, from that in the rheumatic case, and indeed doesn't have to follow any particular pattern at all.

All of mine were operated by the closed technique, 3 from the left side with one resultant insufficiency, 1 from the right side. I did not manage to separate the valve adequately on that last occasion, because the papillary muscles grew fast to the undersurface of the valve and I was unable to cut them with the closed technique. That child will be brought back shortly for an open operation.

I believe that the variances in this pathology strongly demand the open technique, which I am sure Dr. Starkey will and should continue to use. And I would like to point out that whereas we use the right-sided approach for all of our closed operations on the mitral valve, the experiences of my associate, Dr. Henry Nichols, in operating for mitral insufficiency have clearly demonstrated the advantages of the left-sided approach when the open technique is used. Indeed, Dr. Clowes already has pointed out the major advantages, perhaps the most major being the surgeon's ability to remove entrapped air from the ventricle, thus preventing air embolism. It is inevitable that air will enter the left ventricle with an open operation for mitral stenosis.

The real difference in the right- and left-sided approach lies in the difference in the direction of the line of the valve. If you can see it you can easily orient yourself, whether it runs vertically or whether it runs horizontally. The advantage with the right-sided approach in closed operations for mitral stenosis is that the valve presents as an upright "U," whereas from the left-sided approach it lies at a right angle, thus tending to confuse the surgeon and restrain his aggressiveness.

It was a real privilege to hear this very excellent paper.

DR. FREDERICK S. CROSS, Cleveland, Ohio.—Perhaps I am somewhat out of order arising to discuss a previous discussion, but I think there is something extremely important about the approach to the mitral valve, whether it be from the right or left side, that should be emphasized further, and that is the problem of trapped air in the left ventricle.

Last year, in a discussion of one of the papers before this organization, I pointed out in a series of slides that in our opinion, based on both laboratory and clinical experiences, there is less chance for air to be trapped in the left ventricle when the mitral valve is approached from the right side than from the left. Anatomically, the left ventricle is the dependent chamber when the patient is on the operating table with the right side up. Unfortunately, when the valve is approached from the right side, it may be more difficult to work on since the surgeon finds himself somewhat further from his work.

Much of this discussion may be a little beside the point, however, since uniform successful results will be obtained only when one develops that technique which works best in his own hands. The real point of this discussion is that regardless of the approach to the mitral valve, it is extremely important as an added precaution to vent the left ventricle. This vent is kept on gentle suction until the left atriotomy is repaired and the vena caval tapes released to be sure that all residual air bubbles in the left ventricle are removed before turning off the pump-oxygenator and allowing the heart to take over its own function. This maneuver will be a virtual guarantee against air emboli arising from residual air in the left ventricle.

I would like to congratulate the authors on an excellent presentation of an important piece of work, and I appreciate the opportunity to discuss this one important aspect of it.

DR. ROSS ROBERTSON, Vancouver, British Columbia.—Dr. Starkey's paper has interested me immensely. It reminded me of the case of a young woman with a congenital mitral stenosis who survived this lesion, generally lethal to children, because of an associated left superior vena cava emptying into the left superior pulmonary vein. This relieved her mitral stenosis as does the Sweet operation for acquired mitral stenosis. Clinically she was short of breath on mild exertion. There was a continuous murmur over the second left interspace close to the sternum, and also a mitral diastolic murmur.

At operation, the blood could be seen in the distended thin walled left superior vena cava, flowing away from the heart. When the left superior vena cava was clamped, the pressure rose alarmingly in the left auricle, confirming the preoperative diagnosis of mitral stenosis. Consequently, a finger was inserted into the left auricle and found a valve which resembled that described by Dr. Starkey, a kind of membrane with a hole in the middle and no actual commissure. A knife was required to open the valve along a line where the commissures should be located. A mild mitral regurgitation was produced. The left superior vena cava was then clamped without causing an increase in pressure in the left auricle. The clamp was then removed.

The patient made a good recovery and is free of symptoms.

DR EDOUARD D. GAGNON, Montreal, Quebec—I think Dr. Starkey's paper was an excellent one.

I do not wish to discuss points of technique, but I would like to ask him a question on the definition of a congenital mitral stenosis. I ask this question because in the beautiful slide he showed us he had three diaphragmatic stenoses, one of which was slightly funneled and one well funneled, but he showed us, and stated, that they were all *thick* valves.

We have operated on 6 children and 2 of them had these thick valves. Although they had no history of rheumatic fever, we felt that they were acquired, probably due to some other infectious process in childhood. In opposition to these 2, the other children we had to operate on (2 of them with associated coarctation) had valves that were quite different. The leaflets were not thickened at all; there were no commissures that I could recognize. There was a long funnel shaped affair with very short chordae tendineae, inserting right down near the apex of the ventricle. We cut where we thought the commissures should be and the 4 patients did well. The oldest patient we operated upon was 14 years and the youngest was 8 years of age.

We feel that these 4 are the real congenital type, and that the first 2, of the type shown here, were probably acquired, although we couldn't determine what the infectious process was that had scarred the valve leaflets to produce the mitral stenosis.

DR. H. WILLIAM SCOTT, JR, Nashville, Tenn—I, too, would like to congratulate Dr Starkey on bringing this extremely interesting and important problem before the Association. I think it has been the feeling of almost everyone, both internists and surgeons alike, up until very recently, that congenital mitral stenosis represented a relatively hopeless problem from the therapeutic point of view. This had certainly been my understanding.

We have had an opportunity to operate definitively on only 1 patient with congenital mitral stenosis. The nature of the anatomic deformity of the valve was the problem that seemed to us most intriguing, in addition to the question as to whether this might be an acquired lesion of rheumatic origin rather than a congenital one.

Our patient was a 6 year old child with symptoms from birth, a classical presystolic rumbling murmur at the apex and severe pulmonary hypertension. We did the operation using the open technique with the pump oxygenator, and had an opportunity to see that the little valve resembled one of the diagrams shown us by Dr Starkey.

At operation, with the valve exposed, I wanted to find out what the valve felt like, and I used what I thought was very gentle pressure with a finger, simply to assess the edges of the stenotic valve, and I found that the commissures were opened completely simply by the gentle palpation of the operating finger.

We then carefully inspected the little valve and it seemed that what we had divided by digital pressure was a diaphanous membrane with a little slit in it that seemed to fill the orifice between the anterior and posterior leaflets. The valve was otherwise quite normal, as best we could tell, with no evident thickening of it.

I think it would be interesting if Dr. Starkey could bring out to us in his closure of discussion some idea of the anatomic variations of the valve in congenital mitral stenosis, because I think the type of operative procedure that one plans or that one may do should be totally dependent upon the anatomic deformity of the valve.

Our little patient has done fairly well in the 6 months since operation despite a hypoplastic left ventricle, but has not yet had postoperative catheterization studies.

DR. STARKEY (Closing).—I would first like to thank the discussers for their comments and will try to answer some of their inquiries.

As far as the anatomy of congenital mitral stenosis is concerned, there is great variation. It would appear, though, that a considerable degree of subendocardial fibroelastosis is associated with the flat, diaphragmatic type of valve with short or poorly developed chordae tendineae and papillary muscles. This may be associated with considerable hypoplasia of the left ventricle.

The etiology of congenital mitral stenosis is unknown. Fetal endocarditis has been postulated, but I am afraid I have nothing to contribute to this phase of the problem.

The question of surgical approach has been raised by several discussers. I think that for most cases of stenosis or insufficiency that an "open heart" method using a pump-oxygenator is preferable. We favor the right-sided approach to the left atrium. This chamber may be approached satisfactorily either directly anterior to the right pulmonary veins or by way of the right atrium and the interatrial septum. Each method has given an excellent view of the mitral valve.

The child with congenital mitral stenosis who reaches the age of 10 or 12 years seems more likely to have a valve that is funnel-shaped with fused commissures like those of rheumatic mitral stenosis. These are often amenable to surgical relief by the standard, left-sided closed method that one uses routinely in the adult rheumatic patient.

THE ETIOLOGY AND PREVENTION OF ATRIAL FIBRILLATION AFTER MITRAL VALVOTOMY

C Frederick Kittle, M D, and James E Crockett, M D (by invitation),
Kansas City, Kans

THE MOST frequent postoperative complication following mitral valvotomy is the occurrence of atrial fibrillation in a patient with previously normal sinus rhythm This postoperative complication is of particular interest to those concerned with cardiovascular surgery since this arrhythmia may lead to a deleterious tachycardia and a significant reduction in cardiac output We should like to review our experiences with postoperative atrial fibrillation in 254 consecutive patients undergoing mitral valvotomy with particular emphasis on the prevention of this arrythmia

DATA

The clinical records of all patients undergoing mitral valvotomy at the University of Kansas Medical Center and the Kansas City Veterans Administration Hospital since 1953 have been included in this study Excluded are those in whom operative or postoperative fatality occurred or in whom records are incomplete This group consists of 254 patients

Of these 254 there were 99 (39 per cent) who had atrial fibrillation preoperatively and 155 (61 per cent) with a normal sinus rhythm preoperatively Of the 155 patients, there were 41 (26 per cent) who developed atrial fibrillation postoperatively, this being the most common postoperative complication noted with this surgical procedure

Atrial fibrillation in the 41 patients developed as early as the operative day (3 patients) and as late as the fifteenth day, although the majority had the onset of this arrhythmia between the second and fourth postoperative days (Fig 1) No obvious correlation was found between the age of the patients and those in whom fibrillation occurred The youngest patient was 16 and the oldest was 55 years with a mean age of 38

It is of interest that 40 of the 41 patients who fibrillated postoperatively had dynamic mitral stenosis as their main lesion, although several other patients in our series had a normal sinus rhythm and at the time of cardiac exploration

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Supported in part by the Kansas Heart Association and the National Heart Institute

Read at the Thirty ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles Calif April 21 23 1959 were found to have predominantly mitral regurgitation. The 1 patient who did fibrillate with mitral regurgitation was a 16-year-old girl who developed acute rheumatic fever postoperatively and died several weeks later.

The 155 patients with a normal sinus rhythm preoperatively have been divided into four groups: (1) those receiving both digitalis and quinidine, (2) digitalis alone, (3) quinidine alone, and (4) those receiving neither digitalis nor quinidine. Of those receiving digitalis and quinidine the smallest percentage of patients developed atrial fibrillation after operation—9 of 55 patients or 16 per cent. In the group receiving digitalis alone, there were 13 of 43 patients or 30 per cent. In the group receiving quinidine alone, there were 7 of 20 patients or 35 per cent, and in those receiving no medication 12 of 37 patients, or 32 per cent, developed atrial fibrillation.

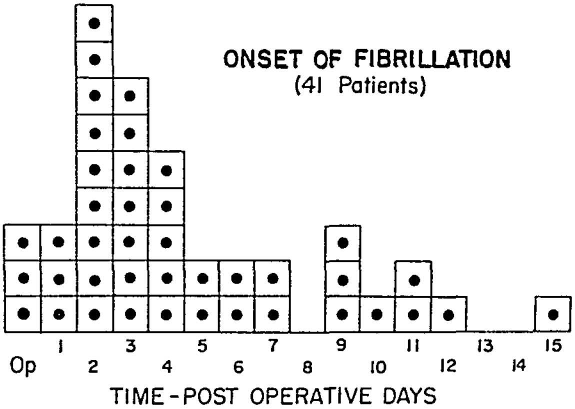

Fig. 1.

In the group of 55 patients receiving both digitalis and quinidine postoperatively as prophylaxis against fibrillation, there were 9 patients who developed fibrillation. In reviewing these particular instances, only 3 were given quinidine judged adequate by our present standards. Although 2 received 0.4 Gm. every 4 hours and 1 received 0.3 Gm. every 4 hours, fibrillation still occurred. The remaining 6 patients were given comparatively meager doses of quinidine, 0.2 Gm. four times daily or 0.2 Gm. every 4 hours.

Of 98 patients who were digitalized postoperatively, 22 fibrillated, an incidence of 22 per cent. Of the 57 patients not digitalized, 19 fibrillated, an incidence of 33 per cent. Thus, the value of both digitalization and quinidinization to prevent postoperative fibrillation would appear substantiated by these statistics.

In the 41 patients who developed atrial fibrillation, there were 3 patients who converted to a normal sinus rhythm spontaneously. These 3 are of considerable interest because their fibrillation began on the operative day, the first postoperative day, and the twelfth postoperative day following an esophagoscopy. Fibrillation in this particular group of 3 patients occurred at unusual times in comparison to other patients who fibrillated. In 5 other patients, no attempt was made to convert the fibrillation to a normal sinus rhythm because of factors which contraindicated quinidine therapy.

In 33 patients an attempt was made to convert the atrial fibrillation to a normal sinus rhythm. In 28 instances this was successful and in 5 it was unsuccessful. Of the 28 who were converted, this was accomplished by quinidinization in 15 patients already digitalized. In 6, conversion was by quinidinization alone, in 5 by postoperative digitalization or extra digitalis, and in 2 by Pronestyl and digitalis. It is believed quite important to convert patients with postoperative atrial fibrillation to a normal sinus rhythm if this can be accomplished.

In the 99 patients who underwent mitral valvotomy with preoperative atrial fibrillation, an attempt to convert to a normal sinus rhythm was made postoperatively in 45. Of these, only 12 were successfully changed to a normal sinus rhythm. Attempts to convert such patients prior to mitral valvotomy have not proved worth while.

DISCUSSION

Atrial fibrillation is a sufficiently common complication of mitral valvotomy to warrant particular attention to its prevention and correction. In a recent article, Heinz and Hultgren[10] reported that 47 per cent of patients undergoing mitral valvotomy with preoperative normal sinus rhythm developed atrial fibrillation postoperatively. In other reviews the incidence has varied from 24 to 38 per cent.[6, 8, 15, 19, 23] Most of the patients described in these articles received digitalis but no quinidine postoperatively.

Atrial fibrillation is a relatively uncommon complication in other postoperative patients who do not have chronic rheumatic heart disease, although it is occasionally seen following thoracotomies. After lobectomy or pneumonectomy in older patients, an incidence between 3.5 and 14 per cent has been noted.[1, 5, 10, 13, 16] In patients who had an intrapericardial pneumonectomy, an incidence of 45 per cent was found by Hurt and Bates.[11] It is significant that only 6 of 43 patients in this study who received quinidine after intrapericardial pneumonectomy developed atrial fibrillation while 10 of 22, who did not, maintained sinus rhythm. Atrial fibrillation is relatively infrequent following operations for congenital heart disease.

Reasons for the development of postoperative atrial fibrillation after mitral valvotomy are not clear. Trauma to the left atrium with subsequent edema and tissue necrosis incident to the valvotomy must be considered an important factor. Others have mentioned the possibility of traumatic pericarditis or postoperative alterations in serum and intracellular electrolytes, but data do not confirm these as etiological factors.[10]

Rheumatic activity as evidenced by histologic findings in the resected atrial appendage has not been found significant in postoperative atrial fibrillation.[6, 10] In our group of 41 patients, the dynamic lesion in 40 was mitral stenosis, although others[10] have stated that atrial fibrillation occurs with greater incidence in patients with mitral regurgitation.

Postoperative atrial fibrillation is a primary concern because of its potential and real danger to the patient.[18] There are many studies to demonstrate that atrial fibrillation significantly reduces the cardiac output.[2, 3, 20, 21]

Hansen and his associates[9] found a decrease of 23 per cent in cardiac output in patients with onset of atrial fibrillation. These patients had well-controlled ventricular rates before and after atrial fibrillation, thus eliminating the variant of ventricular rate as a factor in cardiac output. Conversion to a normal sinus rhythm reduced the pulmonary blood volume and the peripheral venous pressure.

Similarly, Kerkhof[12] found atrial fibrillation to reduce cardiac output by 25 per cent. Corday and his co-workers[4] reported a substantial fall in cardiac output and coronary blood flow with atrial fibrillation. This rapid and appreciable reduction in cardiac output appears the most serious effect of atrial fibrillation. If the ventricular rate reaches 130 to 150 per minute, the cardiac output is even more seriously compromised. Landis and his co-workers[14] have found a disproportionate rise in central venous pressure in dogs after atrial fibrillation began.

In several patients in our group of those who developed postoperative fibrillation, definite evidence of pulmonary edema was noted soon after onset of the atrial fibrillation. The possibility of thrombus formation and embolism would appear increased although we have not observed this.

A considerable difference of opinion exists regarding the role of quinidine in the prevention of postoperative atrial arrhythmias. It is generally conceded that digitalis is of most importance in decreasing and controlling ventricular rate if atrial fibrillation does occur. However, there is no general agreement that digitalis prevents postoperative atrial fibrillation. Wood[23] and Goodwin[8] have expressed the opinion that quinidine is of no value in avoiding this arrhythmia. We believe that combined digitalization and adequate quinidinization are definitely indicated for the prophylaxis of postoperative atrial fibrillation. In our study, those patients receiving both drugs postoperatively had an incidence of atrial fibrillation of only 16 per cent as compared to 30 per cent for those receiving digitalis alone, 35 per cent for those receiving quinidine alone, and 32 per cent for those who received neither drug. The difference among the last three groups are not statistically significant. As noted previously, the majority of those receiving quinidine alone or with digitalis received small amounts of the drug. We now believe that adequate quinidine prophylaxis requires 0.4 Gm. every 4 hours or 2.4 Gm. each 24 hours. This dosage requires daily monitoring by the electrocardiogram, observation of the blood pressure and, when available, serum quinidine levels (Fig. 2).

Conversion of postoperative atrial fibrillation to normal sinus rhythm is much easier than is the conversion of chronic fibrillation. We were able to convert 84 per cent of those with postoperative atrial fibrillation, but only 26 per cent of those with chronic fibrillation. Sellors[19] converted only 1 of 41 with chronic fibrillation while Wood[23] reported a 50 per cent conversion rate in this group although he noted that 40 per cent of these later relapsed to atrial fibrillation.

We have preferred to wait until after the tenth postoperative day to attempt conversion. This allows for healing of the atriotomy and general recovery of the patient. An attempt is made postoperatively to convert all patients to a normal sinus rhythm. To date we have not observed peripheral embolization occurring with or after restoration of sinus rhythm. In patients in whom left atrial thrombus is found that cannot be removed by the usual operative procedure, a re-operation is done utilizing extracorporeal circulation. Following this, when the atrium has been thoroughly cleaned of thrombus, the conversion attempt is made.

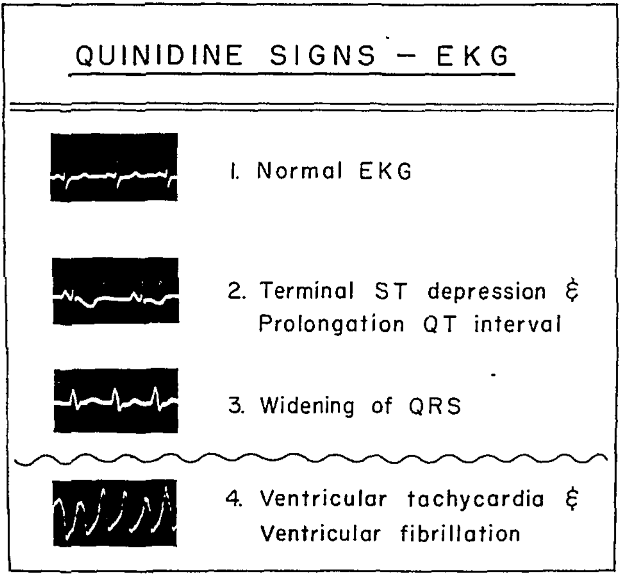
QUINIDINE SIGNS – EKG
1. Normal EKG
2. Terminal ST depression c̄ Prolongation QT interval
3. Widening of QRS
4. Ventricular tachycardia c̄ Ventricular fibrillation

Fig. 2.

In those patients in whom postoperative fibrillation has occurred, quinidine is continued for several weeks with a gradual reduction in dose after dismissal from the hospital. Sudden termination of this drug from a high dosage level may result in a return to atrial fibrillation. In chronic fibrillation, the *quinidine is continued indefinitely if conversion to a normal sinus* rhythm has been accomplished. The maintenance dose is arbitrarily determined from the amount required to effect conversion and the patient's tolerance. Maintenance therapy is necessary to prevent recurrent atrial fibrillation.

SUMMARY

1. Two hundred and fifty-four consecutive patients who had mitral valvotomy are reviewed with particular attention to atrial fibrillation as a postoperative complication.

2. Atrial fibrillation occurred postoperatively in 41 of 155 patients (26 per cent) who had a normal sinus rhythm preoperatively.

3. The arrhythmia developed most commonly on the second, third, or fourth postoperative day.

4. The frequency of postoperative atrial fibrillation was significantly lower in those patients receiving both digitalis and quinidine postoperatively. It is concluded that the combined use of these drugs is beneficial in preventing this deleterious arrhythmia.

5. Local trauma to the left atrium incident to the atriotomy is probably the most important factor in the etiology of this arrhythmia.

6. Conversion of postoperative atrial fibrillation to sinus rhythm can usually be accomplished while conversion of those patients with preoperative atrial fibrillation is more difficult.

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DISCUSSION

DR HARRISON BLACK, Boston, Mass I have enjoyed Dr Kittle's discussion very much It was of interest to me to find this work on the program because we have analyzed some of our experience with this problem in th[illegible] cases at the Peter Bent Brigham Hospital in Boston

(Slide) I might say at the outset that I am alarmed at the size of the quinidine doses employed by Drs Kittle and Crockett It [illegible] ll known that the blood level obtained on similar dosage varies widely from patient t[illegible] nt and that even with the total daily dose of 1 2 Gm serious toxicity and even death [illegible] rred This is only half the dose used in many of Dr Kittle's patients We have em[illegible] two regimens, one with a total daily dose of only 0 8 Gm daily and the other 1 2 Gm [illegible] important point that I would like to make is that, with such do[illegible] results equally as go[illegible] s those of Drs Kittle and Crockett can be obtained I sincerely believe that the higher [illegible] s employed by them need not and should not be used.

In our study [illegible] divided our patients [illegible] ording to our usual clinical classification [illegible] mitral stenosis In Group III of 230 patient [illegible] ho were treated with quinidine, 50 [illegible] an incidence of 22 per cent as contrasted wi[illegible] 42 per cent in the controls This is significant at the 0 1 level of confidence In Group [illegible], however, the use of quinidine reduced the occurrence of postoperative atrial fibrillation only from 62 to 50 per cent—not a significant difference

We also analyzed some of the factors that we thought might have a bearing on the development of this arrhythmia postoperatively, analyzing controls and quinidine patients separately In the control group, there was a significantly higher incidence of fibrillation when there had been prior atrial fibrillation, atrial premature beats, or episodes of palpitation preoperatively The finding of Aschoff bodies in the auricular appendage biopsy and moderate or marked postfracture mitral insufficiency also had a statistically significant influence on the incidence of fibrillation. Recent arthralgia as evidence of rheumatic activity was not statistically important

In the quinidine patients, however, only one of these factors—prior atrial fibrillation, atrial premature beats, or episodes of palpitation—seemed to have any significant influence

As far as quinidine blood levels were concerned, there did not seem to be any important difference between those who fibrillated and those who did not On the first postoperative day those who fibrillated had an average level of 4 61 [illegible] normal [illegible] them had an average value of 4.4 [illegible] onset of atrial fibrillation as possible [illegible] after [illegible] critical importance

Summing up, we can say that, in Group III, [illegible] quinidine [illegible] the incidence of postoperative atrial fibrillation [illegible]

42 to 22 per cent. Of those who fibrillate, 36 per cent will revert spontaneously when their rate is slowed by increasing digitalis dosage. (I should mention parenthetically that it is our practice to digitalize all patients before mitral surgery and carry them on maintenance digitalis postoperatively.)

Of those who do not revert spontaneously, 89 per cent can be reverted with quinidine in about 10 days after operation. Therefore, if we start with 100 patients who are in normal sinus rhythm, who are digitalized and on quinidine preoperatively, there will be postoperative fibrillation in 22, spontaneous reversion in 8. Of 14 who remain in atrial fibrillation, 12 can be reverted and only 2 will leave the hospital with an irregular rhythm.

DR. JEROME R. HEAD, Chicago, Ill.—Dr. Kittle's very interesting paper has interested me, although I am not a cardiac surgeon, as I am sure it has interested everyone who is a cardiac surgeon and is a thoracic surgeon.

We have had, after pneumonectomies and lobectomies, our share of postoperative fibrillations. We have come to be able, I believe, to anticipate them. In older people, whose coronary circulation is poor, we use quinidine prophylactically.

There is one point in the etiology that I would like to bring up, and that is why I am discussing this paper. That is the importance of adequate respiratory toilet after surgery, and of an ample supply of oxygen. In 1 patient who fibrillated after surgery and did not raise his secretions and became progressively worse, we did a tracheotomy and put him on a pump respirator. As we slowed down the respirator we could make him fibrillate; as we speeded up the respirator the fibrillation would stop.

This led us to what seems to me to be a very reasonable conclusion, that the oxygen in the blood plays an important part in postoperative fibrillation. Since that time we have been able to convert a number of patients with postoperative atrial fibrillation simply by using a nasal catheter and cutting down their activity.

DR. LAURENCE K. GROVES, Cleveland, Ohio.—We have not used the prophylactic quinidine, but I believe we use quinidine postoperatively about as has been shown. I am neither a cardiologist nor a pharmacologist, but little mention was made of the toxicity of quinidine. Down on the bottom of the last slide there was a little comment about ventricular arrhythmias, and I am sure that with the help of our cardiologists we have killed at least 1 patient by steadily increasing the dose in refractory fibrillation postoperatively. Nothing was found in this gentleman at postmortem after being found dead in bed, but I presume that he had ventricular fibrillation.

DR. MAX G. CARTER, New Haven, Conn.—Like the last discusser, I come merely because I am trying to learn.

Our cardiologists are at the moment rather insistent that we not give prophylactic quinidine, and I would like to ask Dr. Kittle about this problem. Some years ago we felt that people with arteriosclerotic heart disease, who were going to have esophagectomies or pneumonectomies, should have prophylactic digitalis and we used it and had very few arrhythmias. We have since stopped that, and I am sure we don't have any more arrhythmias than formerly.

In the cardiac patients, however, digitalis is given only when there is a specific indication, and in the patients who come to operation with a normal rhythm, if there is not an indication, digitalis is not given. If they then begin to fibrillate, digitalis is given with a view to getting them fully digitalized within the first 24 hours. If they do not convert, then quinidine is added immediately.

This has seemed reasenable to me purely on the advice of the cardiologists. They point out, I think correctly, that digitalis and quinidine are both toxic drugs, and, in some of these patients who have a markedly impaired myocardial reserve, one may get into more trouble using it than in not using it.

We have had a lot of experience demonstrated this morning, and I would like to hear how Dr. Kittle feels about this problem.

DR CHARLES P BAILEY, Philadelphia, Pa—I wasn't going to join the discussion, but I feel so strongly about digitalis that I thought I should

Our cardiologists for a long time had the same feeling as Dr Carter "There is no use in giving digitalis unless there is impending heart failure, auricular fibrillation or something of that sort" The trouble is, they forget that we in our surgery often produce heart failure, or so reduce the reserve of the heart that it is practically in failure That is when the patients need the digitalis If you have not given it in advance you then have to give it intravenously It then takes 20 minutes, which may be too long

We have had to use ouabain and other rapidly acting glucosides to save some of these people right under our eyes during open heart surgery There is no question but that some of the hearts just would not beat effectively and that they could not be taken off the pump until these glucosides took effect We are convinced of the great value of "prophylactic" digitalis in all patients undergoing any kind of heart surgery This has been substantiated in many laboratories in experimental work in animals, the results showing a much higher survival rate in certain operations on the heart when digitalis is used routinely than when it is not We ought to take advantage of our animal experiences and bring clinical medicine at least up to the experimental level

DR KITTLE (Closing)—I am grateful to all of the discussers for their remarks I think postoperative atrial fibrillation is an extremely important problem Because of the wide variety of patients who are being subjected to operation, this is a problem that can be settled only by a careful statistical analysis of large series The more critical appraisal there is in each particular clinic, the sooner we are going to come to a definite answer about this problem

One problem was raised the danger of using quinidine Quinidine is certainly a dangerous drug But against the danger of quinidine we are balancing the danger and the risk of the patient who suddenly develops postoperative atrial fibrillation We cannot ignore the patients after lobectomy or pneumonectomy who have a normal sinus rhythm and develop atrial fibrillation Most of us have seen some of these patients die because of the reduction in cardiac output that does occur as a result of this arrhythmia, so that if we can prevent atrial fibrillation I think means should be taken to do this

(Slide) When quinidine is given it is quite important to appraise these patients daily, to watch their blood pressure several times each day and, most important, to monitor the electrocardiogram There are definite changes that occur with quinidine dosage, and certainly these changes occur before we get to any fatal arrhythmia such as ventricular tachycardia or ventricular fibrillation

These are the changes, briefly described here Beginning with the normal electrocardiogram, first there is a terminal depression of S T segment and a prolongation of the Q T interval This subsequently progresses to a widening of the QRS interval Nausea, scotomata, or subjective symptoms are not considered an indication for decreasing or stopping quinidine

Of all patients in whom quinidine was given, we have had only 1 patient who developed ventricular tachycardia Fortunately this patient had no further serious difficulty This developed in a rather unusual situation because this patient was receiving Banthine We believe that because of the Banthine the absorption of quinidine was altered so that a higher blood level than usual developed

I think we cannot ignore the factor of trauma to the left atrium as a cause for postoperative fibrillation because in the past month we have seen 2 patients with normal sized left atria who had left atriotomies, 1 for the removal of a myxoma, another for an anastomosis of an anomalous left pulmonary vein Both patients developed atrial fibrillation postoperatively Neither had left atrial hypertension preoperatively

RELATIVE ANTIHEPARIN POTENCY OF POLYBRENE AND PROTAMINE IN PATIENTS UNDERGOING EXTRACORPOREAL CIRCULATION

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Jane Telford, M.D., Houston, Texas

THE PRINCIPAL safety factor in the use of heparin to prevent coagulation of blood in several clinical situations has been the availability of an antagonist to treat overdosage or for prompt cessation of heparin effects when necessary. This antagonist, protamine sulfate, has been prompt, reliable, and predictable in its action. However, a number of undesirable side actions have followed its use, including dyspnea,[1] hypotension, bradycardia and, when given in excessive dose in vitro, an increase instead of decrease in coagulation time.[2]

In 1953, Preston and Parker[3] reported on the effectiveness of polybrene, a synthetic polymerized quaternary ammonium salt, as a heparin antagonist in vitro and in vivo, and estimated that 0.75 mg. of polybrene would neutralize 1.0 mg. of heparin. Weiss and his co-workers[4] reported the effective use of polybrene to neutralize heparin administered during extracorporeal circulation for open heart surgery. They also suggested that 0.7 mg. of polybrene was sufficient to antagonize the anticoagulant effect of 1 mg. of heparin. When administered to conscious patients, polybrene produced subjective effects described as a "colloid reaction," which included symptoms as dizziness, flushing of the face, dyspnea or wheezing, substernal pressure, lumbar pain, and weakness.

The present study was designed to determine the relative merits of protamine and polybrene as antagonists to heparin used during extracorporeal circulation. The proper comparison of drugs with similar primary actions requires that a precise estimate be made first of the relative potency of the drugs being compared.[5] Only then can relative side action liability be determined using equipotent doses. The failure to employ equipotent doses in studies of side action liability can lead to large errors in estimates of relative merits of drugs. This study was designed in this pattern.

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METHODS

Antiheparin Potency.—Forty noncyanotic patients undergoing extracorporeal circulation with a bubble oxygenator[6] for corrective open heart surgery were subjects for this assay. These patients included both children and adults and a variety of cardiac diseases (age range, 3 to 28 years, weight range, 22 to 136 pounds). Clotting times were determined by the Lee White method, using 1.0 c.c. volume of blood in each of 3 tubes. The first tube was tilted every minute until a clot formed. Then the second tube was tilted similarly, then the third. The clotting time was the period between sampling of the blood and the time when the blood in all three tubes had clotted. All blood samples were collected from the right ventricle in dry 10 c.c. syringes with a 20 gauge needle. Samples were drawn at the following periods: (1) prior to heparinization, approximately 20 minutes before cardiopulmonary bypass, (2) 5 minutes after heparin administration, (3) 5 minutes after administration of the heparin antagonist, approximately 10 minutes after cardiopulmonary bypass, (4) 15 minutes after administration of the antagonist, and (5), in some patients, 5 minutes after administration of additional heparin antagonist.

The following doses of heparin antagonists were studied: protamine 1.5 mg., 2.0 mg., and 5.0 mg. per kilogram of body weight, polybrene 0.75 mg., 1.5 mg., and 3.0 mg. per kilogram of body weight. Prior to administration of either antagonist, 10 per cent calcium gluconate (0.5 to 1.0 Gm.) was administered intravenously to neutralize any citrate possibly circulating from banked blood administered prior to bypass. Both antagonists were injected in undiluted form over a period of 30 to 60 seconds. The usual time elapsing from the administration of heparin to administration of antagonist was 30 to 40 minutes.

In all patients, heparin (1.5 mg./Kg.) prolonged coagulation time by more than 60 minutes beyond the control (pre-heparin) clotting time. Assuming a 100 per cent heparin effect to be 60 minutes beyond control clotting time, the following formula was devised to express antiheparin potency following administration of an antagonist:

$$\% \text{ heparin neutralization} = \frac{(\text{control clotting time} + 60) - \text{observed clotting time}}{60}$$

Side Action Liability.—Eleven adult patients recovering from minor surgical procedures done under local or spinal anesthesia (without vasopressor) were subjects of this study. Undiluted protamine (5 mg./Kg.) or polybrene (3 mg./Kg.) was injected rapidly intravenously over a period of 30 to 60 seconds. Immediately before and after injection, blood pressure, pulse rate, and respiratory rate were recorded every minute for 5 minutes, then every 5 minutes for 20 minutes. Changes in pulse rate of less than 10 per minute, or of systolic or diastolic pressure of less than 10 mm. Hg were not considered significant. The subjective effects produced by the drug were elicited by responses to nonspecific questions as "How do you feel?"

RESULTS

Relative Potency.—When the degree of heparin neutralization by both protamine and polybrene was compared at 5 and 15 minutes after administration (Table I), it was apparent that maximum antiheparin effect occurred with both drugs within 5 minutes. Therefore, clotting times 5 minutes after administration were used to determine relative potency. The 5-minute post-neutralization data as collected are presented in Table II. Except for the group which received 1.5 mg./Kg. of protamine, the duration of cardiopulmonary bypass was comparable in all groups as was the control clotting times in groups being compared. Per cent heparin neutralization was calculated for each individual and the means in Table II represent the means of individual values.

TABLE I. COMPARISON OF DEGREE OF HEPARIN NEUTRALIZATION AT 5 AND 15 MINUTES AFTER INTRAVENOUS ADMINISTRATION OF PROTAMINE AND POLYBRENE

DOSE (MG./KG.)	NUMBER OF PATIENTS	MEAN % HEPARIN NEUTRALIZATION 5 MIN. AFTER ADMINISTRATION	MEAN % HEPARIN NEUTRALIZATION 15 MIN. AFTER ADMINISTRATION
		Protamine	
1.5	3	21.7	26.7
2.0	2	71.5	50.0
5.0	5	98.4	98.4
		Polybrene	
0.75	5	24.2	15.0
1.5	5	96.0	92.0
3.0	7	100.7	97.3

TABLE II. EFFECTIVENESS OF THREE DOSE LEVELS OF PROTAMINE AND POLYBRENE IN NEUTRALIZING THE ANTICOAGULANT EFFECTS OF 1.5 MG./KG. OF HEPARIN

DOSE (MG./KG.)	NUMBER OF PATIENTS	DURATION OF BYPASS MIN. ± S.E.†	CONTROL CLOTTING TIME MIN. ± S.E.†	CLOTTING TIME 5 MIN. AFTER ANTAGONIST MIN. ± S.E.†	% HEPARIN NEUTRALIZATION* ± S.E.†
			Protamine		
1.5	5	7.8 ± 0.7	14.4 ± 2.6	54.6 ± 7.8	21.6 ± 13
2.0	6	12.4 ± 2.5	15.2 ± 3.1	31.7 ± 6.8	72.3 ± 11
5.0	5	14.4 ± 2.6	9.2 ± 0.5	10.2 ± 1.0	98.4 ± 2.3
			Polybrene		
0.75	5	14.4 ± 2.8	15.6 ± 3.7	61.0 ± 9.8	24.2 ± 15
1.5	11	13.5 ± 1.9	14.5 ± 1.7	16.5 ± 2.7	96.6 ± 3.1
3.0	8	16.9 ± 2.6	9.6 ± 0.4	9.5 ± 0.3	100.3 ± 0.9

*See text for definition.
†Standard error of mean.

These data were plotted as a dose effect relationship for each drug (Fig. 1), utilizing only the data of the two lower dose levels from each drug. The regression equation for each curve was calculated from a plot of individual values. The slopes of the two curves were strikingly similar and significant (polybrene: slope 96.6, $P < 0.01$; protamine: slope 101.7, $P < 0.02$). Covariance analysis of this block of data[7] indicated no significant difference between regression ($P > 0.05$) but a highly significant difference between curve means ($P < 0.01$). Because of the similar regression coefficients, curves were not adjusted to a common slope and relative potency was estimated by calculation at 100 per cent heparin neutralization. This estimate was 1.54 mg./Kg. of polybrene or 2.27 mg./Kg. of protamine neutralized 1.5 mg./Kg. of heparin in this clinical situation. Expressed differently, polybrene was 1.5 times as potent as protamine at 100 per cent neutralization effect.

Additional data to support this estimate were obtained by the administration of additional doses of polybrene to patients whose clotting times did not return to control values after the initial dose of antagonist. In 4 patients, polybrene (1.5 mg./Kg.) given after protamine (1.5 mg./Kg.) increased heparin neutralization from 27 to 99 per cent. In 3 patients, polybrene (1.5 mg./Kg.) given after protamine (2.0 mg./Kg.) increased neutralization from 63 to 102 per cent. In 5 patients, polybrene (0.75 mg./Kg.) given after polybrene (0.75 mg./Kg.) increased heparin neutralization from 24 to 65 per cent. In 2 patients, who received polybrene (1.5 mg./Kg.), an additional dose of polybrene (1.5 mg./Kg.) did not significantly increase the degree of neutralization.

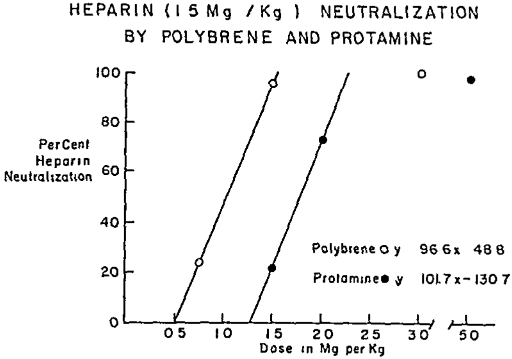

Fig. 1.—Relative antiheparin potency of polybrene and protamine expressed as a dose effect relationship. At 100 per cent heparin neutralization 1.54 mg. per kilogram of polybrene is equivalent to 2.27 mg. per kilogram of protamine. At twice the neutralization dose neither drug produces an anticoagulant effect.

Since excessive doses of protamine and polybrene have been reported to produce a heparin-like effect and prolong coagulation times,[2, 6] the effects of twice the estimated neutralizing dose was also studied. Five patients received 5 mg./Kg. of protamine and 8 patients, 3 mg./Kg. polybrene (Table II). Obviously, no anticoagulant effect was produced by these doses.

When used for cardiopulmonary bypass, the pump oxygenator itself can induce clotting defects from trauma to the blood with consequent loss of fibrin and thrombocytes. It was, therefore, important to correlate the duration of perfusion with the degree of failure of heparin neutralization. This was done with the data of 16 patients in whom heparin effects were not completely antagonized by either antagonist. The correlation coefficient of the relationship between per cent heparin neutralization (range 0 to 75 pe

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2.0	2	71.5	50.0
5.0	5	98.4	98.4
		Polybrene	
0.75	5	24.2	15.0
1.5	5	96.0	92.0
3.0	7	100.7	97.3

TABLE II. EFFECTIVENESS OF THREE DOSE LEVELS OF PROTAMINE AND POLYBRENE IN NEUTRALIZING THE ANTICOAGULANT EFFECTS OF 1.5 MG./KG. OF HEPARIN

DOSE (MG./KG.)	NUMBER OF PATIENTS	DURATION OF BYPASS MIN. ± S.E.†	CONTROL CLOTTING TIME MIN. ± S.E.†	CLOTTING TIME 5 MIN. AFTER ANTAGONIST MIN. ± S.E.†	% HEPARIN NEUTRALIZATION* ± S.E.†
		Protamine			
1.5	5	7.8 ± 0.7	14.4 ± 2.6	54.6 ± 7.8	21.6 ± 13
2.0	6	12.4 ± 2.5	15.2 ± 3.1	31.7 ± 6.8	72.3 ± 11
5.0	5	14.4 ± 2.6	9.2 ± 0.5	10.2 ± 1.0	98.4 ± 2.3
		Polybrene			
0.75	5	14.4 ± 2.8	15.6 ± 3.7	61.0 ± 9.8	24.2 ± 15
1.5	11	13.5 ± 1.9	14.5 ± 1.7	16.5 ± 2.7	96.6 ± 3.1
3.0	8	16.9 ± 2.6	9.6 ± 0.4	9.5 ± 0.3	100.3 ± 0.9

*See text for definition.
†Standard error of mean.

These data were plotted as a dose effect relationship for each drug (Fig. 1), utilizing only the data of the two lower dose levels from each drug. The regression equation for each curve was calculated from a plot of individual values. The slopes of the two curves were strikingly similar and significant (polybrene: slope 96.6, $P < 0.01$; protamine: slope 101.7, $P < 0.02$). Covariance analysis of this block of data[7] indicated no significant difference between regression ($P > 0.05$) but a highly significant difference between curve means ($P < 0.01$). Because of the similar regression coefficients, curves were not adjusted to a common slope and relative potency was estimated by calculation at 100 per cent heparin neutralization. This estimate was 1.54 mg./Kg. of polybrene or 2.27 mg./Kg. of protamine neutralized 1.5 mg./Kg. of heparin in this clinical situation. Expressed differently, polybrene was 1.5 times as potent as protamine at 100 per cent neutralization effect.

Additional data to support this estimate were obtained by the administration of additional doses of polybrene to patients whose clotting times did not return to control values after the initial dose of antagonist. In 4 patients, polybrene (1.5 mg./Kg.) given after protamine (1.5 mg./Kg.) increased heparin neutralization from 27 to 99 per cent. In 3 patients, polybrene (1.5 mg./Kg.) given after protamine (2.0 mg./Kg.) increased neutralization from 63 to 102 per cent. In 5 patients, polybrene (0.75 mg./Kg.) given after polybrene (0.75 mg./Kg.) increased heparin neutralization from 24 to 65 per cent. In 2 patients, who received polybrene (1.5 mg./Kg.), an additional dose of polybrene (1.5 mg./Kg.) did not significantly increase the degree of neutralization.

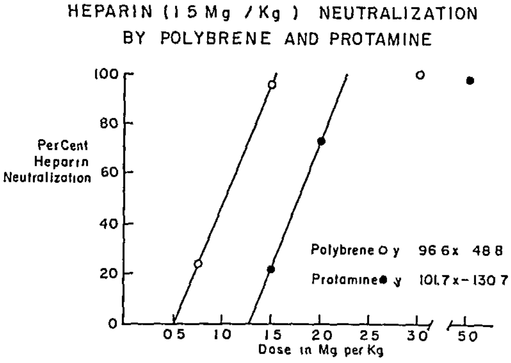

Fig. 1.—Relative antiheparin potency of polybrene and protamine expressed as a dose effect relationship. At 100 per cent heparin neutralization 1.54 mg. per kilogram of polybrene is equivalent to 2.27 mg. per kilogram of protamine. At twice the neutralization dose neither drug produces an anticoagulant effect.

Since excessive doses of protamine and polybrene have been reported to produce a heparin-like effect and prolong coagulation times,[2, 8] the effects of twice the estimated neutralizing dose was also studied. Five patients received 5 mg./Kg. of protamine and 8 patients, 3 mg./Kg. polybrene (Table II). Obviously, no anticoagulant effect was produced by these doses.

When used for cardiopulmonary bypass, the pump oxygenator itself can induce clotting defects from trauma to the blood with consequent loss of fibrin and thrombocytes. It was, therefore, important to correlate the duration of perfusion with the degree of failure of heparin neutralization. This was done with the data of 16 patients in whom heparin effects were not completely antagonized by either antagonist. The correlation coefficient of the relationship between per cent heparin neutralization (range 0 to 75 per cent) and duration of perfusion (range 5.0 to 22.5 min.) was 0.098. This indicated that no correlation existed and that other clotting defects which may have been produced by the pump-oxygenator probably did not account for the failure of clotting after administration of low doses of heparin antagonists.

The heparinized blood used in the pump-oxygenator contained 18 mg. of heparin per 500 c.c. It was therefore possible that the actual amount of heparin being neutralized in this study was more nearly 2.0 mg./Kg. than 1.5 mg./Kg. Assuming a 70 kilogram man has 5 liters of blood, the dose of 18 mg. of heparin per 500 c.c. of blood approximates an in vivo dose of 2.5 mg./Kg. The actual effective circulating heparin at the end of perfusion could therefore range between 1.5 and 2.5 mg./Kg. The exact amount would depend on the blood volume of the patient, the blood volume of the extracorporeal circuit, and the loss of heparin during blood storage.

Side Action Liability.—In the 40 patients used for the potency assay, both protamine and polybrene were injected intravenously undiluted over a period of 15 to 60 seconds. The injection was timed to follow immediately upon the removal of the cannulae from the venae cavae, if the pulse rate and blood pressure were stable and satisfactory. Marked hypotension did not occur in any patient following the rapid administration of either drug at any dose level. In some patients, decreases in systolic blood pressure of 10 to 20 mm.Hg were observed at some time during the 10-minute period which followed the administration of an antagonist. However, these pressure changes could be as readily attributed to the continuing blood loss from the cardiotomy incision as to the injection of the drug, since these events were simultaneous. When hypotension occurred, it was treated by transfusion. No patient received a vasopressor following cardiopulmonary bypass and no electrocardiographic changes could be attributed to the injection of these drugs.

The data obtained from the 11 postoperative patients given protamine and polybrene are summarized in Table III. Large doses (twice the neutralizing dose) and rapid injections were used to magnify any changes which might occur. It is obvious that both drugs did surprisingly little. Protamine tended to have a greater hypotensive effect than polybrene. The blood pressure of one patient given protamine decreased from 120/70 to 90/60 mm. Hg and remained low for 20 minutes when a vasopressor was given. No alarming effects appeared in any patient. Most changes, including all symptoms, lasted less than 5 minutes and occurred primarily during 1 or 2 minutes after rapid injection.

DISCUSSION

When given in equipotent doses, both protamine and polybrene are effective heparin antagonists. After intravenous administration, both drugs exert their maximum effect within 5 minutes. Heparin neutralization by either drug was sustained, since no patient required additional amounts of protamine or polybrene in the postoperative period and clotting times, done one hour postoperatively, were in the normal range. From this study a precise statement

TABLE III. SIDE ACTION LIABILITY OF INTRAVENOUS PROTAMINE AND POLYBRENE IN CONSCIOUS SUBJECTS

	DRUG	
	PROTAMINE (5 MG./KG.)	POLYBRENE (3 MG./KG.)
Subjects	6 (ages 16-57)	5 (ages 21-62)
Total Dose mg. c.c.	 270-450 mg. 27-45 c.c.	 180-230 mg. 18-23 c.c.
Blood pressure change	Decreased in 6 Mean decrease 19 mm. systolic 9 mm. diastolic Duration—5 min. in 4 Duration—5 to 20 min. in 2	Decreased in 1 140/70 to 120/70 for 2 min. No change in 4
Pulse rate change	No change in 2 Increased (25/min.) in 4 Duration—5 to 10 min. in 4	Decreased (12/min.) in 2 Increased (25/min.) in 3 Duration—5 min. in 5
Respiration	No change in 6	No change in 4 Hyperventilation in 1
Symptoms (no. of subjects)	Bad taste—1 Flushed face—2 Arm pain—1 Stinging all over—1 No effect—3	Bad taste—3 Substernal discomfort—1 Restlessness—1 Generalized muscle spasm—1 No effect—1

as to the dose of protamine or polybrene required to neutralize 1.0 mg. of heparin cannot be made since the exact amount of effective circulating heparin at the end of extracorporeal circulation could not be determined. However, a precise estimate of the relative antiheparin potency of protamine and polybrene can be made, namely, polybrene is 1.5 times as potent as protamine at 100 per cent antiheparin effect.

In both anesthetized and awake patients protamine and polybrene are remarkably free from serious side actions. Even with rapid intravenous injection, at twice the neutralizing dose, in patients who had undergone extracorporeal circulation, no marked hypotension resulted. In conscious subjects, protamine tended to produce more hypotension than polybrene, but the hypotension was not severe in any patient. The subjective effects produced by both drugs were unpleasant, but mild and transient. Except for hyperventilation in one instance after polybrene, no dyspnea, wheezing, bronchospasm, or allergic phenomena were observed in these patients. There was no evidence of an anticoagulant effect from large doses of protamine or polybrene. Both drugs have a wide margin of safety.

Heparin is administered intravenously to our patients at 1.5 mg. per kilogram of body weight just before cannulation for bypass. In order to antagonize heparin we currently administer 2.5 mg. to 3 mg. per kilogram of polybrene rapidly intravenously upon the removal of the cannulae from the venae cavae. This has proved satisfactory and safe. Our preference for polybrene is based primarily on ease of administration and, secondarily, on a lesser hypotensive effect. Polybrene is packaged in a 10 c.c. ampule containing 100 mg., whereas protamine is contained in a 5 c.c. ampule at the same concentration. Therefore, fewer ampules of polybrene are required for the adult patient and a smaller volume can be injected because of increased potency. In addition, polybrene solution shows no tendency to foam as does protamine. When blood replacement has been adequate, hypotension following protamine has not been a problem in our experience.[9] Others, however, have been troubled by "protamine shock."[2] We have chosen a polybrene dose greater than 1.5 mg./Kg. because of its safety and in order to ensure complete heparin neutralization since it is possible that circulating heparin after extracorporeal circulation may be as high as 2.5 mg./Kg.

SUMMARY

In 40 patients undergoing extracorporeal circulation, the relative antiheparin potency of 3 dose levels of polybrene and 3 dose levels of protamine have been determined by Lee-White clotting times after administration of 1.5 mg./Kg. of heparin. At 100 per cent heparin neutralization, polybrene was 1.5 times as potent as protamine. Heparin neutralization by both drugs after rapid intravenous administration was maximum within 5 minutes and was sustained. The side actions produced by these drugs were noted in anesthetized patients and in 11 conscious adults. Protamine tended to produce mild hypotension in conscious subjects whereas polybrene produced no such response. Subjective effects produced by both drugs at twice the heparin neutralization dose were mild and transient.

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COARCTATION OF THE AORTA WITH PROXIMAL AORTIC DILATATION AND CALCIFIC ATHEROMATOUS DEGENERATION CORRECTED BY ENDARTERECTOMY

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DILATATION and degenerative changes of the aorta lying proximal to a coarctation are frequent findings in the surgical repair of this congenital anomaly In a study of 200 collected cases of adult coarctation, Abbott[1] described proximal aortic dilatation and atheromatous degeneration to a greater or lesser extent in 50 per cent of the cases When these changes in the aortic wall are pronounced, the difficulties of operative correction and the incidence of postoperative hemorrhage are appreciably increased The accepted procedure of resection and anastomosis in such cases presents a formidable surgical problem, generally accompanied by a high operative mortality In the case reported herein, a successful correction of a coarctation associated with severe dilatation and calcific atheromatous changes in the proximal aorta was accomplished by employing a modification of the technique of endarterectomy This case is presented as a successful example of the use of an alternate method in the treatment of this particular surgical problem

CASE REPORT

The patient was a 27 year old white married woman who was referred to the University of California Medical Center, Los Angeles, in Oct 1957, for evaluation of a known hypertension of 7 years' duration Hypertension was first diagnosed in 1950 by her family physician when a blood pressure of 190/80 mm Hg was recorded during a routine physical examination A thorough work up in 1951 at a metropolitan New York hospital revealed that the patient had always been asymptomatic, active physically, and had progressed normally through two pregnancies Further work up at that time revealed a blood pressure of 165/65 mm Hg in the right arm and 108/70 mm Hg in the right leg She was a well developed, well nourished woman with the only positive findings limited to her cardiovascular system She had bilateral bounding carotid pulses and a Grade 2 systolic murmur audible over the entire precordium The heart was not enlarged Femoral pulsations were markedly diminished bilaterally An electrocardiogram showed a vertical electrical axis with a normal sinus rhythm Roentgenogram of the chest demonstrated advanced calcific sclerosis and dilatation of the ascending aorta and the aortic arch and its branches, terminating several centimeters distal to the left subclavian artery No

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notching of the ribs was visible. An angiocardiogram of the right side of the heart was normal. An aortogram, however, revealed a markedly dilated, proximal aorta, 40 mm. in diameter, which narrowed to 17 mm. in diameter in the descending aorta. The impression recorded in 1951 was that the patient had hypertension of the upper extremities with marked atherosclerosis of the proximal aorta and probable coarctation. Since 1951, the patient had been on antihypertensive drugs and had remained well except for increasing fatigability and mild exertional dyspnea.

On admission to this institution in 1957, the patient's blood pressure in each arm was 240/70 mm. Hg and in each lower extremity was 110/75 mm. Hg. The femoral pulsations were barely palpable. A blowing, Grade 4 systolic murmur was heard over the precordium, which transmitted into the neck and axilla. A Grade 2 early diastolic murmur was audible along the left sternal border in the fourth interspace. An electrocardiogram revealed left ventricular hypertrophy. A moderate cardiomegaly was present on roentgenogram, and the previous severe calcific atherosclerosis of the proximal aorta associated with diffuse dilatation and prompt narrowing of the aorta, distal to the left subclavian artery, was again visualized (Fig. 1). Intravenous pyelograms and renal chemistries were normal. Serological tests for syphilis were negative. The preoperative diagnosis was coarctation of the aorta with extensive proximal calcific sclerosis and dilatation, cardiomegaly, and aortic insufficiency.

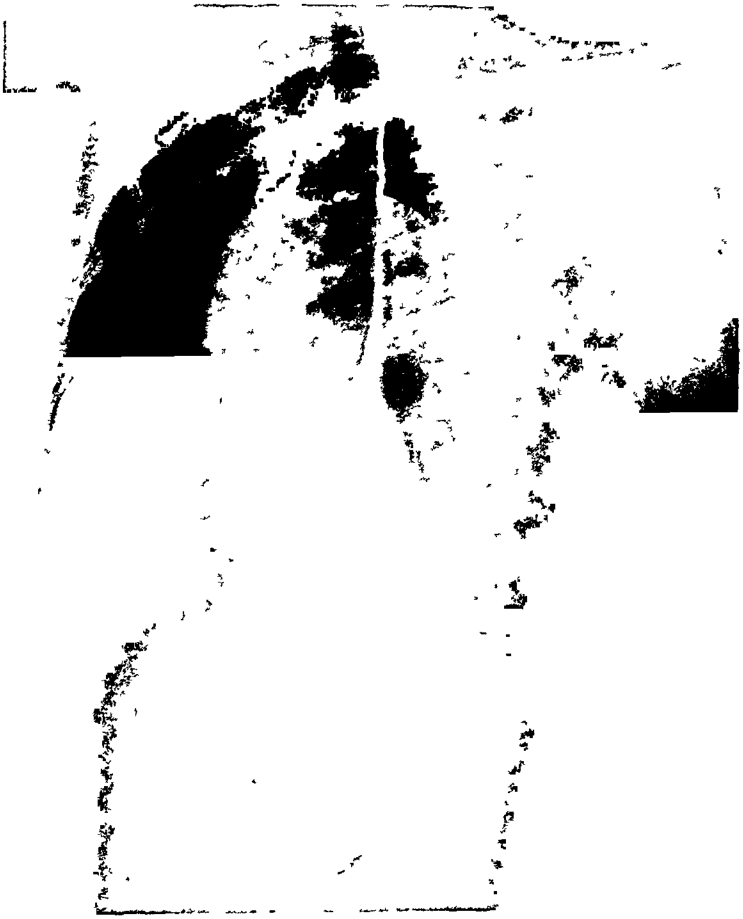

Fig. 1.—Left anterior oblique chest x-ray demonstrating marked dilatation and calcification of proximal aorta and aortic arch branches.

On Jan. 10, 1958, a left posterolateral thoracotomy was made through the bed of the fifth rib, and the fourth and sixth ribs were divided posteriorly. A very dilated calcific

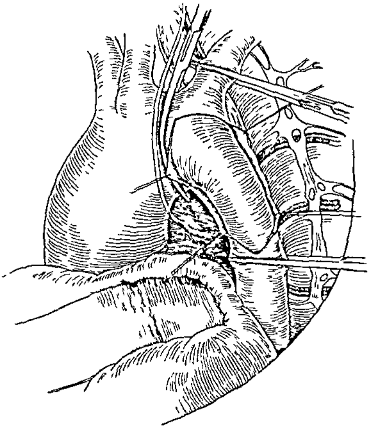

Fig 2.

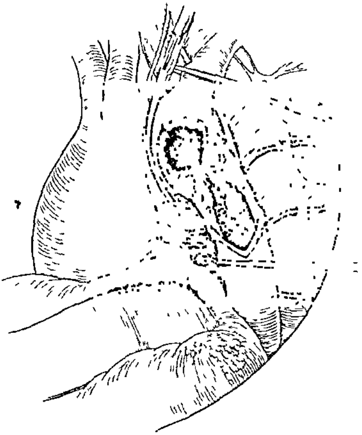

Fig. 3.

Fig. 2.—Left posterolateral thoracotomy. The visceral pleura is incised over the coarctation segment. The discrepancy in vessel diameter in the proximal and distal aorta is demonstrated

Fig. 3 —Aortotomy over the coarctation revealing heavy calcific atheromatous plaque deposition in the proximal aorta and stenotic area with almost total obstruction of the aortic lumen.

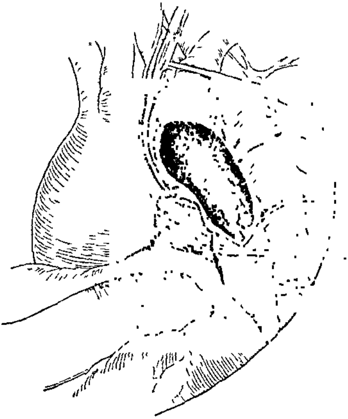

Fig. 4.

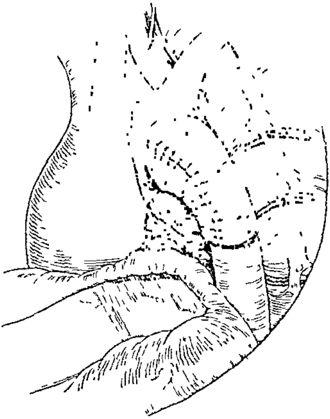

Fig. 5.

Fig. 4.—Aortic lumen restored to an adequate diameter following endarterectomy of obstructing process.

Fig. 5.—Aortic homograft sutured over thinned-out wall and aortotomy.

aorta extended from the aortic valve to 1 cm. distal to the left subclavian artery; at this point, the aorta narrowed to one third its proximal diameter with a faint pulsation distally (Fig. 2). The strictured area did not resemble a typical coarctation, since its external diameter was only slightly less than a normal-sized descending aorta. The intercostal arteries were moderately dilated. After the left subclavian artery and proximal and distal aorta were controlled, a longitudinal aortotomy was made through the area of coarctation. The lumen was almost totally obstructed with atheromatous deposits which lined the stenosed segment of aorta (Fig. 3). The obstructing calcific deposits were freed from the aortic wall by sharp and blunt dissection to a point just proximal to the left subclavian artery. A lumen of 1.5 to 2.0 cm. was obtained through the stenosed area (Fig. 4). The aortotomy was closed with a continuous 3-0 silk suture and reinforced with an aortic homograft, since the aortic wall was extremely thin in the endarterectomized segment (Fig. 5). During the occlusion of the proximal aorta, Arfonad maintained the blood pressure in the upper extremities below 200 mm. Hg.

The patient tolerated the operative procedure quite well, and her postoperative course was uncomplicated. Simultaneous brachial and femoral artery pressure of 250/78 and 215/80 mm. Hg, respectively, were recorded postoperatively. The patient is now one year postoperative and blood pressures taken at this time are 158/54 mm. Hg in the right arm and 180/100 mm. Hg in the right leg. The patient leads a normal life at the present time and has begun lessons in water skiing.

DISCUSSION

The dilatation and degenerative changes observed in the aorta proximal to a coarctation are generally believed to result from stresses of increased intraluminal pressure. Clagett[2] felt that the degree of vascular damage in the proximal aorta is related directly to the duration of the lesion. He found that the patients with coarctation with extensive vascular damage had an average age older than those with minimal or moderate damage. He also postulated that the degree of vascular damage was related to the amount of physical exertion and resultant strain on the cardiovascular system, since the more extensive changes were present predominantly in males.

Another possible factor in the etiology of these changes in the vessel wall is an inherent weakness in the media of the aortic wall itself. It is difficult to determine whether the elastic fiber deficiency and fibrous replacement described in the proximal aorta in young adults with coarctation is congenital in origin or secondary to stress.[3-5] It would be necessary to study the aorta in infants and children with coarctation, presumably before intraluminal pressure would have had any effect, in order to postulate a congenital weakness underlying these changes in the vessel wall.

In the case reported, severe dilatation and calcification of the proximal aorta prohibited the usual procedure of resection and anastomosis. Since the circumference of the strictured segment was only slightly less than normal, it was felt that the obstructive process could be removed intraluminally through a longitudinal aortotomy. The progressive accumulation of calcified deposits on a previously congenitally stenotic area resulted in an almost complete aortic obstruction. We feel that this patient never had a typical coarctation, but rather a congenital narrowing of the aorta distal to the left subclavian artery which was probably compatible with normal life expectancy until she acquired pronounced secondary changes in the proximal vessel wall and coarctation segment itself.

Thromboendarterectomy has been employed more extensively in recent years in the attack on occlusive arterial disease. Favorable experience has accumulated using this technique in arteriosclerotic occlusive disease of the aortic, iliac, femoral, renal, carotid, and coronary arteries. The usual type of coarctation, with its pronounced narrowing of the entire diameter of the aortic wall, is only correctible by resection. However, in situations where the size of the coarctation segment is larger and the changes in the vessel wall are pronounced, endarterectomy may be employed successfully with less risk to the patient.

SUMMARY

The successful correction of a coarctation of the aorta, associated with severe dilatation and atheromatous degeneration of the proximal vessel wall, remains a hazardous surgical problem. In the case reported, the proximal aorta as well as the coarctation segment were involved with calcific atheromatous degeneration. The constricted segment was restored to an adequate lumen by a longitudinal aortotomy and endarterectomy. This operative approach, although not applicable in the majority of cases of coarctation, is recommended as an alternate procedure in selected patients.

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TREATMENT AND PALLIATION OF CARCINOMA OF THE ESOPHAGUS BY TWO-STAGE ESOPHAGECTOMY AND ESOPHAGOCOLOGASTROSTOMY

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Carcinoma of the esophagus, in most cases, is a fatal tumor; it is difficult to palliate, and is a challenge to all interested in the disease.

Watson and associates[1] reviewed 993 cases seen at Memorial Center in New York and found only a 2 per cent over-all 5 year survival rate. The cause for low salvage rate for patients with this disease is due to several reasons. Many times it is due to failure of the patient to consult his physician at the onset of trouble. In other instances, it is due to the physician's failure to study thoroughly and diagnose the case. A vital factor, however, is the problem of insufficient resection which results in incomplete removal of the esophagus and its metastatic extensions. Scanlon, Morton, Walker, and Watson[2] have pointed out that carcinoma of the esophagus frequently extends through the submucosal lymphatics, beyond the gross limits of tumor, and in a group of 79 patients who had esophagectomy, 45.6 per cent had inadequate removal of the esophagus because tumor was present in the edge of the specimen or in submucosal lymphatics in that area.

The only answer to the above deficiency lies in total esophagectomy similar to the Torek procedure. By utilizing this principle, and using the colon to replace the esophagus as an esophagocologastrostomy, one can do a more thorough operation for cancer. It also provides excellent palliation for incurable cases and, if done in two stages, the procedure is clinically safe.

We have utilized the above-mentioned principle in 13 cases of carcinoma of the esophagus or upper stomach. In 5 of the 13 cases, at the time of thoracotomy, the lesion was found to be nonresectable so esophagocologastrostomy was done as a palliative procedure. Two deaths resulted after attempts to do esophagocologastrostomy and esophagectomy as one-stage procedures. These deaths precipitated our decision to adopt the two-stage operation because usually the poor condition of the patient will not permit the entire procedure to be done

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at one time with reasonable safety Esophagocologastrostomy and resection in two stages have been completed in 3 patients A brief summary of our total experience follows

REPORT OF CASES

Case 1—(JGH 278877) C F, a woman 56 years of age, was admitted on July 31, 1956, because of dysphagia Roentgenograms disclosed an obstructing lesion in the mid esophagus, and the specimen taken for biopsy through the esophagoscope showed squamous cell carcinoma Esophagocologastrostomy and resection of the entire esophagus was done in one stage, utilizing two surgical teams Regardless of treatment, the patient went into shock and died on the second day following surgical intervention

Permission was not given for necropsy

Case 2—(BMH 235636) P B, a 59 year old woman, was admitted on Dec 7, 1956, with a complaint of dysphagia An epidermoid carcinoma of the esophagus had been diagnosed in 1955, roentgen therapy had been given and gastrostomy done She apparently responded well to roentgen therapy but could not swallow On Dec 21, 1956, an esophagocologastrostomy was done, the colon was brought into the neck through a retrosternal tunnel The patient recovered and was able to take a regular diet for 2 years She died 26 months after surgery

Case 3—(BMH 238220) R B, a man 42 years of age, was admitted on Jan 8, 1957, complaining of throat pain of 2 months' duration Roentgen study revealed a tumor in the distal esophagus This was confirmed by esophagoscopy, and biopsy showed the tumor was an adenocarcinoma

Surgical exploration revealed an extensive tumor involving the lower esophagus and upper stomach Esophagogastrectomy and esophagocologastrostomy were done with the colon brought through the esophageal hiatus, and the esophagocolic anastomosis was made high within the thorax

The patient recovered from the operation, but he had a difficult postoperative course which was marked by development of localized empyema This patient died 10 months later, but during that period he had no difficulty eating his food

Case 4—(BMH 257618) J T, a 78 year old woman, was admitted July 15, 1957, with a history of progressive dysphagia of 6 weeks' duration The patient was found to have carcinoma of the cardia involving the lower esophagus At surgical exploration, the lesion was found to be nonresectable so an esophagocologastrostomy was done with the colon brought into a retrosternal position

The patient died of cardiac complications on the ninth day following the operation

Case 5—(JGH 295983) N W, a woman 49 years of age, was admitted on Aug 12, 1957, complaining of progressive dysphagia Studies revealed a squamous cell carcinoma of the upper and middle esophagus

A one stage total esophagectomy and esophagocologastrostomy were carried out with the colon brought into the neck through a retrosternal tunnel The patient seemed to tolerate the procedure well but suddenly went into progressive shock and died on the second postoperative day

Permission for necropsy was refused

Case 6—(JGH 296007) T M, a man 58 years of age, was admitted on Aug 26, 1957, complaining of dysphagia of one month's duration Studies confirmed a diagnosis of squamous cell carcinoma of the upper esophagus

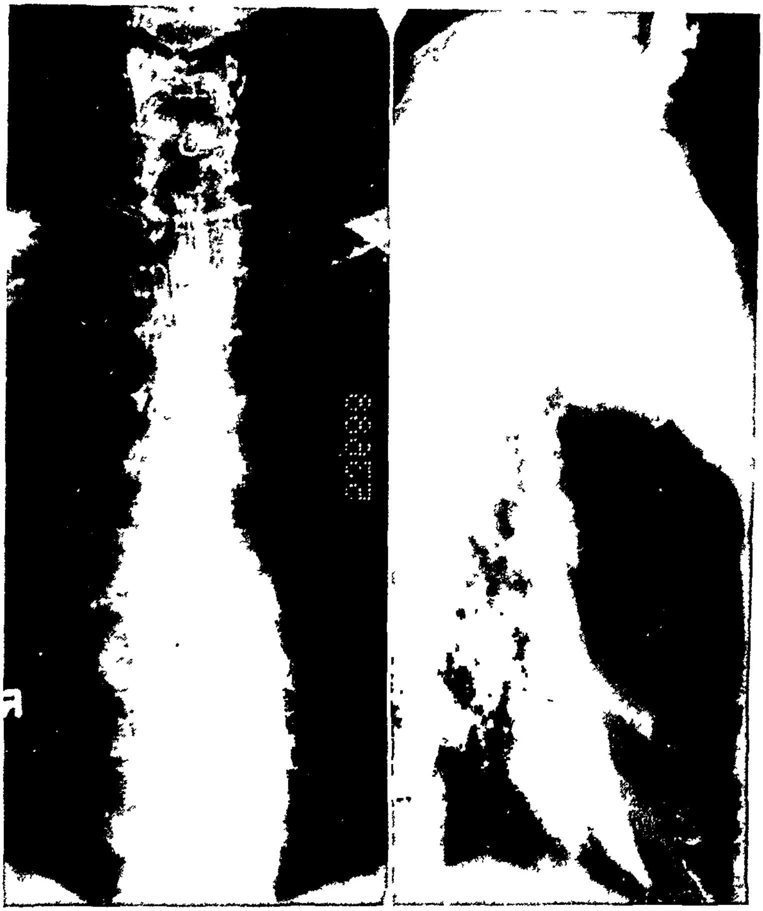
This patient was operated on in two stages At the first stage, an esophagocologastrostomy was done with the colon brought into the neck retrosternally The patient had some temporary anorexia but was taking a soft diet by the twelfth postoperative day

One month after the first stage operation, a total esophagectomy was done. He was dismissed in good condition on the eighth day and was taking a regular diet.

Cobalt teletherapy was given postoperatively.

The patient died 7 months later. He was able to eat without difficulty, but during the last month of his life he developed anorexia.

Case 7.—(JGH-132966.) E. S., a 49-year-old man, was admitted on Aug. 8, 1957, with a chief complaint of progressive dysphagia. Studies revealed that he had a squamous-cell carcinoma of the middle esophagus.



A. *B.*

Fig. 1.—Case 9. *A*, Preoperative esophagogram showing constrictive lesion at the junction of the middle and lower thirds of the esophagus.
B, Postoperative view of the substernal colon. Emptying was so rapid the picture resembles an air contrast enema.

As a first stage surgical operation, an esophagocologastrostomy was done, and the colon was brought into the neck through a retrosternal tunnel. Two weeks after this procedure, a total esophagectomy and repair of an inguinal hernia were done. When the patient was discharged 9 days later he was able to eat a regular diet.

He received cobalt teletherapy later and, when last seen 7 months after his hospital dismissal, he was doing well and had gained fourteen pounds.

Case 8.—(JGH-92928.) W. B., a 57-year-old man, was admitted in August, 1957, complaining of cough on deglutition. He was found to have carcinoma of the esophagus with a malignant tracheoesophageal fistula A Levin tube was placed into the stomach and the patient was dismissed.

He was readmitted on Sept 29, 1957, and a palliative esophagocologastrostomy was done He did well for one week and was eating a regular diet when a fistula developed at the esophagocolic anastomosis An unsuccessful attempt was made to close this fistula so a gastrostomy was done He was last observed in January, 1958, and was doing poorly.

Case 9—(BMH 275132) H. G, a man aged 59, was admitted with a complaint of dysphagia of 3 months' duration Studies revealed a carcinoma of the middle esophagus (Fig 1, *A*)

An esophagocologastrostomy was done as a first stage operation (Fig 1, *B*) and his recovery was uneventful except for a small fistula in the neck which closed in 3 days The patient was able to eat well and insisted on returning home 3 weeks after surgery

He returned one month later; a thoracotomy was done, but his lesion was nonresectable.

Cobalt therapy was given. The patient died 10 months later, but he was able to eat until the time of his death.

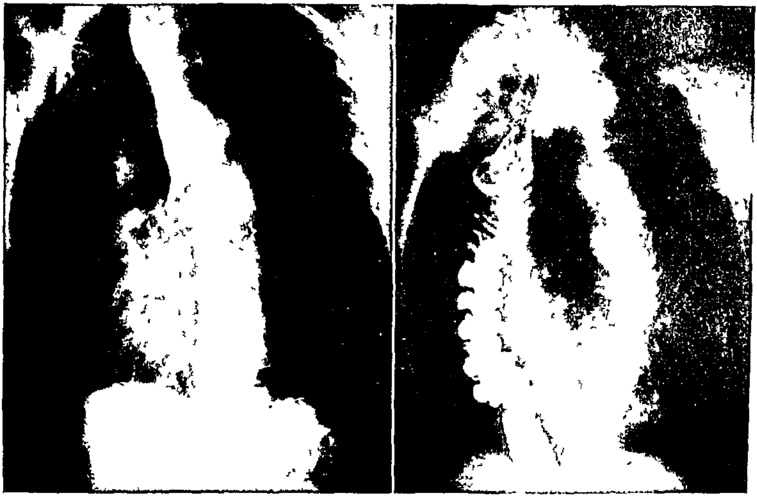


Fig 2—Case 12 *A*, Esophagogram showing a large lesion in the middle third of the esophagus

B, Postoperative esophagocologram showing free passage of barium through the anastomosis and colon

Case 10—(BMH 271106) W S, a man 66 years of age, was admitted on Nov. 18, 1957, complaining of dysphagia of 4 months' duration Studies revealed a squamous cell carcinoma in the upper esophagus

The patient had an esophagocologastrostomy performed on Nov 25, 1957, when the colon was brought up into the neck through a retrosternal tunnel.

A subsequent separation of the abdominal wound was resutured on Dec. 5, 1957

On Dec 18, 1957, a thoracotomy proved the lesion was nonresectable. The patient was discharged on a soft diet and was eating well The patient was still living at follow up in November, 1958

CASE 11.—(JGH-307878.) E. W., a woman 52 years of age, was admitted with a chief complaint of dysphagia of one month's duration. She was found to have a squamous-cell carcinoma of the middle esophagus. This patient was also found to have bilateral arteriosclerotic obstruction of the carotid arteries.

Bilateral carotid endarterectomy was done first, and one month later an esophagocologastrostomy was done. The patient died 3 weeks later. The necropsy revealed multiple cerebral infarcts to be the cause of death.

CASE 12.—(JGH-254278.) W. K., a man 67 years of age, was admitted on Jan. 3, 1958, with a complaint of dysphagia of 2 months' duration. Studies revealed a squamous-cell carcinoma of the middle esophagus (Fig. 2, *A*).

On Jan. 16, 1958, he had an esophagocologastrostomy (Fig. 2, *B*) and this was followed by a total esophagectomy on Feb. 6, 1958. He recovered from these procedures and was dismissed from the hospital on Feb. 29, 1958.

He was readmitted on June 27, 1958, with a complaint of nausea and vomiting, and roentgenogram showed gastric retention. A gastroenterostomy was done and he recovered satisfactorily.

He was last seen on Aug. 1, 1958, at which time he was eating a regular diet and had gained three pounds.

CASE 13.—(BMH-286387.) S. W., a man aged 65, was admitted on April 13, 1958, with a complaint of dysphagia which he had had for 3 months. Studies revealed an adenocarcinoma of the esophagogastric junction.

On April 23, 1958, an esophagocologastrostomy, along with a pyloroplasty and gastrostomy, were performed. When he had a thoracotomy 2 weeks after those procedures, the esophagogastric junction was resected but a tracheotomy was necessary in the immediate period following operation because of excessive tracheal secretions. The patient recovered and was dismissed on June 15, 1958, at which time he was taking a soft diet. He died 7 months later of carcinomatosis.

TECHNIQUE

We have abandoned the one-stage total esophagectomy and esophagocologastrostomy for treatment of carcinoma of the esophagus, and now prefer to do an esophagocologastrostomy as the first stage surgical operation and a total esophagectomy as the second stage. The esophagectomy can usually be done within 2 weeks after the first stage has been done. The technique of the first stage procedure follows.

The patient is admitted to the hospital a few days before he is to have operation, and the colon is cleansed by enemas and purgatives; it is sterilized by Neomycin and one of the nonabsorbable sulfa drugs.

At operation, the patient is placed in the supine position, and a long, midline incision is made. The right colon is mobilized and an appendectomy is done. The ileocolic and right colic vessels are divided, care being taken to preserve the marginal vessels and middle colic vessels. The colon is divided in its transverse portion to the left of the midline, and the ileum is divided at the ileocecal junction and the distal ileum is closed by inversion. This is followed by an ileotransverse colostomy, and when this anastomosis is begun, a second team of surgeons begins its procedure in the neck.

An incision is made along the inner margin of the sternomastoid muscle on the left side; the cervical esophagus is mobilized and divided just above the thoracic inlet, and the distal portion is inverted, closed, and allowed to drop back into the mediastinum A retrosternal tunnel is then developed by blunt dissection with the fingers, care being taken so the pleura will not be torn On occasion we have resected the medial end of the clavicle to enlarge the thoracic inlet The retrosternal tunnel is developed simultaneously from the abdominal end by another team of surgeons until a space is obtained from neck to abdomen which will admit the colon without tension or compression The colon, cecum first, is then passed behind the stomach, into the tunnel, and into the neck It is usually necessary to both gently push and pull the colon through the tunnel, and a long thread in the cecal end is pulled from above, thus assisting the passage of the bowel The cecum is then anastomosed to the esophagus using interrupted silk sutures in two layers, and the anastomosis of the distal colon into the anterior wall of the stomach is placed as high as is technically feasible A pyloroplasty or pyloromyotomy is then done A Levin tube may be passed through the colon, but since this is fairly difficult to accomplish, we usually have eliminated a tube completely or inserted one through a gastrostomy

The patient is allowed to have surgical liquids on the third or fourth day following operation and, if his progress is satisfactory, he is given a soft diet in one week

The second stage of the operative procedure involves resection of the entire esophagus from the previously closed cervicomediastinal portion down to the esophagogastric junction This is through a right thoracotomy incision in the fifth or sixth interspace depending upon the level of the lesion The esophagectomy is usually quite easy, atraumatic for the patient, and can be done in an hour or less The patient usually can be dismissed about 6 to 8 days after this stage

MORTALITY AND COMPLICATIONS

Two of our patients who had one stage procedures developed shock after operation and died This caused us to stage the procedure, and we have had no other patient develop this complication One patient developed cardiac failure and died Another patient who died had esophagocologastrostomy subsequent to bilateral carotid endarterectomies Necropsy determined that this patient had multiple cerebral infarcts We believe that in this case the complications properly should be ascribed to the previous carotid artery surgery

Two patients each developed an esophageal fistula in the neck One fistula *closed promptly, but the other failed to close and resulted in failure of the* operation

Other complications encountered were localized empyema in one case, wound separation in one case, excess tracheal secretions necessitating tracheotomy in one case and late pyloric obstruction in one case

DISCUSSION

Numerous methods have been used to replace or substitute for the esophagus after esophagectomy, but all methods have had their limitations and und features. Until recently the most commonly used method of esophageal substitution was the use of the stomach which was mobilized and drawn up into the chest. The major disadvantage of this method was the resultant peptic esophagitis in about 60 per cent of the cases.

Regurgitation and anorexia are additional problems to cope with after esophagogastrostomy. The higher the lesion is located in the esophagus, the greater becomes the problem of inadequate blood supply, and the greater the risk of surgical mortality.

The use of jejunal loops is attended by high incidence of difficulties with blood supply and, if the anastomosis is in the thoracic cavity, the mortality is high.

The construction of skin tubes and similar procedures has never become popular because of the time, expense, and numerous operations necessary to carry a case to completion.

Kelling[3] and Vulliet,[4] in 1911, working independently, apparently were the first to utilize the colon as an esophageal substitute. Von Hacker,[5] in 1914, and Roith,[6] in 1923, reported cases in which the colon was used as a substitute for the esophagus.

Ochsner[7] reviewed the literature from 1911 to 1934 and found 20 cases of subcutaneous colon transplants. This type of operation did not become popular until improved colon sterilization became possible, but in the past 5 years, numerous cases have been reported in the literature. This procedure lends itself to cases of esophageal atresia, esophageal stricture, esophageal obstruction due to malignancy, and to cases requiring esophageal resection. The transplantation may be accomplished by employing the right and transverse colon, the transverse colon alone, or the left colon. The colon may be brought into the thorax via the esophageal hiatus, through a separate opening in the diaphragm, or through a retrosternal or subcutaneous tunnel. Advantages of using the colon in this manner follow.

1. The blood supply of the colon usually allows one to mobilize a sufficient length to reach the pharynx and still have adequate circulation to the distal end. This makes it superior to the jejunum as a replacement part because the blood supply of the jejunum is often not sufficient to allow one to mobilize a long segment.

2. The colon is apparently resistant to acid peptic digestion. Ivy,[8] Wangensteen,[9] and others have shown that the colon's resistance to gastric secretion is greater than that of the jejunum or the esophagus. In approximately 75 cases of esophagocologastrostomy which we have found reported in the literature, or have knowledge of, there has been only one in which marginal ulceration has occurred.[10] This is in contrast to cases in which the stomach is anastomosed to the esophagus and in which nearly 60 per cent develop acid peptic esophagitis.[11]

3. The use of the colon has another advantage in that the stomach remains in its normal location, performing its normal function as a reservoir, and not functioning as a transit tube. We believe this is the reason why the patient

who has had esophagocologastrostomy has fewer digestive disturbances and better nutrition than the patient who has had esophagogastrostomy We have formulated our impression from experience gathered from 20 cases of esophagocologastrostomy which were done for various conditions

With the use of the colon as replacement for the esophagus, in nearly all cases, one is able to bring the colon to the neck, and thus an anastomosis can be made in the neck instead of in the chest If leakage should occur, only a small local abscess and/or fistula develops in the neck However, if anastomosis is made in the chest and leakage occurs, empyema and severe sepsis can result and this complication carries a high mortality rate We feel that in most cases the colon should be brought through a retrosternal tunnel into the neck and anastomosis made there instead of in the intrapleural space

The original Torek operation which removes the esophagus and leaves an esophageal fistula and gastrostomy is the more satisfactory operation for esophageal cancer than any since described because it provides for a wide resection of the esophagus The disadvantage of esophageal fistula and gastrostomy now is corrected readily by esophagocologastrostomy Scanlon, Morton, Walker, and Watson have recently advocated return to the Torek procedure, and we concur with them

We have chosen to do the esophagocologastrostomy as the first stage procedure instead of first resecting the esophagus We made this choice because we have observed that in most cases of carcinoma of the esophagus, the nutrition of the patient is very poor, and this best can be corrected by furnishing the patient a route for swallowing rather than by gastrostomy Second, in many instances, esophagocologastrostomy is palliative, and we feel it would be difficult to convince patients that a second major operation must be done after finding a nonresectable lesion at thoracotomy as the first stage

Theoretically, one first should remove the neoplasm and delay reconstruction until later, however, we feel that the 2 week delay between stages does not result in significant increased metastases or shortened patient survivals

One of the disadvantages of treatment by roentgen therapy in the past has been the complication of stricture in the area of the neoplasm We hope that creating a channel for deglutition in an area far removed from the lesion being treated will allow more intensive roentgen treatment for patients with nonresectable lesions More intensive treatment should also be possible for those receiving treatment after resection Only more experience and observation will teach us if this is an advantage

RESULTS

The results in our series of 13 cases are listed in Table I

Four patients died in the postoperative period Two of these died of shock and because of this experience, we have abandoned the use of the single stage esophagocologastrostomy and esophagectomy One patient died of cardiac failure and one of cerebral infarction

Although our mortality rate is high, blame, in part, can be laid to the fact that many of these patients are poor risks due to malnutrition, vitamin deficiency, and similar conditions. Also, one expects some higher degree of morbidity and mortality when performing a new type of procedure. We feel that staging the procedures and more operating experience will decrease our operative mortality and morbidity. This has been true in our more recent experience.

TABLE I

CASE	LOCATION OF LESION	PROCEDURE	RESULTS
1	Mid-esophagus	Esophagocologastrostomy and resection in one stage	Postoperative death
2	Upper esophagus	Esophagocologastrostomy and roentgen therapy	Lived 26 months
3	Low esophagus and stomach	Esophagocologastrostomy and resection in one stage	Lived 10 months
4	Low esophagus and stomach	Esophagocologastrostomy	Postoperative death
5	Upper esophagus	Esophagocologastrostomy and resection in one stage	Postoperative death
6	Upper esophagus	Esophagocologastrostomy and resection in two stages	Lived 7 months
7	Middle esophagus	Esophagocologastrostomy and resection in two stages	Alive and eating well
8	Middle esophagus with tracheoesophageal fistula	Esophagocologastrostomy	Unimproved due to cervical fistula
9	Middle esophagus	Esophagocologastrostomy and roentgen therapy; lesion nonresectable at thoracotomy	Lived 10 months
10	Upper esophagus	Esophagocologastrostomy; lesion nonresectable at second stage	Living 1 year later
11	Middle esophagus	Esophagocologastrostomy	Postoperative death (cerebral infarction)
12	Lower esophagus	Esophagocologastrostomy and resection in two stages	Alive and eating well 7 months postoperative
13	Lower esophagus and upper stomach	Esophagocologastrostomy and resection (palliative) in two stages	Lived 7 months

SUMMARY

1. Because of submucosal extension of carcinoma of the esophagus, many patients who have had subtotal esophagectomy have had inadequate resection.

2. The Torek procedure, combined with reconstruction, utilizing the right and transverse colon, in suitable cases, offers a better operation for cancer.

3 In nonresectable cases, esophagocologastrostomy results in the best palliation we have observed with reference to swallowing, weight gain, and freedom from undesirable side effects

4 The use of the colon in esophagoplasty we believe, is preferable to the use of the stomach or jejunum

5 Eleven cases of carcinoma of the esophagus and 2 cases of carcinoma of the esophagogastric junction have been treated by esophagocologastrostomy combined with resection

6 Four of the aforementioned patients died in the immediate period following surgical operation, 2 developed esophagocutaneous fistulas, one of which closed in 3 days Other complications were reversible and were corrected

7 The patients who survived the operative procedures obtained excellent palliation, and we believe that the patients who have had resection have a better chance for a cancer cure

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THE RELATION OF ANTECEDENT TUBERCULOSIS TO BRONCHOGENIC CARCINOMA

A Study of the Tuberculin Test, Radiologic and Pathologic Evidences

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Since the first description of coexistent bronchogenic carcinoma and pulmonary tuberculosis by Bayle in 1810,[1] there have been several interpretations regarding the association of these two diseases. Interest in this problem has been stimulated by the recognized increase of bronchogenic carcinoma and the search for an etiologic agent. In an attempt to investigate further the possible connection between the two diseases, this present study was begun. A series of patients with primary bronchogenic carcinoma was compared with a control group with respect to the tuberculin skin test. This same group was studied radiologically to determine how often the calcified, primary tuberculous complex was associated anatomically with tumor; and both lesions were classified as to segmental location. This segmental localization of bronchogenic carcinoma was confirmed by the examination of an additional series of resected pulmonary carcinomas and, in a portion of these, a search was made for both calcified and noncalcified tuberculous foci.

Although Bayle usually is credited with the first documentation of these two diseases in the same patient, he used the term "phthisic," without pathologic proof, to describe a clinical state. Therefore, Penard,[2] in 1846, may have reported the first case of coexistent bronchogenic carcinoma and pulmonary tuberculosis. Since then, besides individual case reports, the literature has been concerned with three general theories: that tuberculosis and carcinoma are (1) antagonistic, (2) related coincidentally, and (3) definitely associated.

Antagonism.—Rokitansky,[3] in 1854, stated that the two diseases were antagonists since neither seemed to affect the same organs. The problem was analyzed statistically by Pearl,[4] in 1929, with a study of 6,670 postmortem records from the Johns Hopkins Hospital. In 816 autopsies of patients dying from a malignancy, 6.6 per cent had associated tuberculosis, as opposed to 16.3 per cent in the same number of persons dying from diseases other than a

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malignancy. Conversely, 1.2 per cent of 886 autopsies on persons dying from tuberculosis had a cancer as opposed to 9.13 per cent in the same number dying from diseases other than tuberculosis. He supported Rokitansky's view, and even suggested treating carcinoma with iatrogenic tuberculosis. In the same year, Carlson and Bell[5] challenged Pearl's interpretation since patients usually have only one major disease; there must be more cases of tuberculosis among patients without cancer (including tuberculosis as a disease group) than in those with cancer. Then, in addition to verifying Pearl's statistics, they also noted that healed tuberculous lesions were found with approximately the same frequency in patients with cancer, active tuberculosis, and heart disease (as an arbitrary control group). Hueper[6] reviewed the previous literature and came to the conclusion that the two diseases were antagonistic, notwithstanding Carlson and Bell's conclusions. Recently, Desmueles[7] has reported the rarity, in his experience, of associated pulmonary tuberculosis and bronchogenic carcinoma.

Coincidence.—In 1932, Cooper[8] summarized the previous literature, and reported 24 cases of coexistent diseases. He concluded that "nearly all observers are agreed that healed tuberculous lesions are found with equal frequency in cases with carcinoma and in cases without carcinoma. Therefore, apparently, a latent tuberculous infection is without bearing on the development of malignant tumors." He also felt that the same was true of active tuberculosis. Earlier, Hoffman[9] reported that he could find no association and, in 1938, Holman[10] remarked " . . . usually there is no evidence of anatomic relationship between the two processes, and more often than not the tuberculous lesions are entirely inactive." Stein[11] expressed the same opinion but presented no data. Dymalski[12] reported that in 15 (20 per cent) of 56 cases of bronchogenic carcinoma there were acid fast bacteria on sputum analysis, but on pathologic examination only one third of these demonstrated active tuberculosis. In one half, no demonstrable tuberculous focus could be identified other than calcified nodes. He concluded that the association of the two diseases was fortuitous since he believed 10 to 20 per cent of adults dying of causes other than carcinoma of the lung have acid fast bacteria in the sputum, and approximately 5 to 10 per cent of the population of the United States harbor living tubercle bacilli.

Definite Association.—In 1919, Broders[13] summarized all the available literature and found that the two diseases were associated in 16.3 per cent. He felt the facts did not support Rokitansky and suggested that pathologists were not searching specifically for healed tuberculous foci. Ewing, in 1928, stated that tuberculosis was the chief etiologic factor in bronchogenic carcinoma, but later modified that view (1940).[14] Barron[15] incriminated old tuberculous scars and cavities as precancerous lesions, and Fried supported this opinion. He reported that 10 per cent of pulmonary carcinomas were associated with tuberculosis[16] and, in a presentation of 13 cases,[17] named the proliferation of bronchial epithelium into tuberculous cavities as the exciting cause of carcinoma. In his opinion, old scars were invaded secondarily. Robbins,[18] quoting unpublished data, reported that 5 per cent of 100 bronchogenic carcinomas at autopsy were associated with active tuberculosis and, in presenting 11 cases, found only 2 in which the tumor arose from an old fibrocaseous focus. In the remaining specimens, the tuberculous foci were either distal to the neoplasm or far removed from it. The view that carcinoma activates previous tuberculous lesions has been supported by Nuessle,[19] whereas the opposite view has been stressed by Woodruff,[20] who, in 67 cases, studied the anatomic relationship between pulmonary carcinomas and calcified nodules. The association was considered significant if the nodule was (1) greater than 4 mm. in size, (2) in the same lobe or lymph nodes draining the same lobe as the tumor, and (3) larger than any other nodules in the opposite lung. With the use of ante- and postmortem x-rays he noted that 79 per cent of epidermoid, 60 per cent of anaplastic, and 17 per cent of adenocarcinomas were associated closely with calcified nodules. He pointed out that the possible etiologic factors secondary to tuberculosis could be bronchial irritation by calcified lymph nodes, parenchymal scarring by a healed focus, local bronchiectasis aiding the localization of tars from cigarette smoke, and the carcinogenic activity of cholesterol frequently seen in healed foci. Schwartz[21] believes that tuberculosis is the chief etiologic factor in bronchogenic carcinoma. In a pathologic study, he has found carcinomas related to bronchial scars presumably the result of tuberculous bronchitis or adenitis. Certainly tuberculous nodes can affect adjacent bronchi, and Haggenmuller[22] has reported that, in 8.7 per cent of 987 cases of thoracic lymph node tuberculosis, there were radiologic signs of atelectasis secondary to bronchial compression or obstruction. The tubercle bacillus has been cited as causing carcinoma in mice in a single experimental study.[23] Cruickshank[24] has shown statistically that the distribution of tuberculosis closely follows that of bronchogenic carcinoma in adjacent population areas in England. Westergren[25] recently reported that 33 per cent of 100 cases of bronchogenic carcinoma developed in a part of the lung which had been previously the site of a tuberculous process. In 11 cases there was the possibility of direct association.

Minute peripheral tumors have been described by several investigators. Raeburn[26] found small, asymptomatic, malignant tumors adjacent to lung scars. He believes many carcinomas have a bronchiolar origin arising as malignant change in reparative bronchiolar hyperplasia. This has been noted to occur in association with scars of healed tuberculosis, infarcts, and foreign bodies among others. This epithelial change has been termed "benign atypical proliferation" by some authors[27] although there are 3 cases of proved lymph node metastases.[29] Raeburn has demonstrated the early spread of cancer from these peripheral growths to regional lymph nodes and lobar bronchi, thereby appearing primary in these hilar structures. Prior and Jones[30] have described minute peripheral tumors, one associated with a healed tuberculous scar. James and Pagel[31] described 2 cases of superior sulcus tumors arising from calcified apical plaques. Other observers have reported microscopic foci of tumor cells in the peribronchial fibrosis accompanying bronchiectasis.[28] These have resembled oat cell tumors, quite distinct from the bronchial squamous metaplasia associated with bronchiectasis, which has been shown rarely to cause carcinoma.[32] In these collected studies, the malignant nature of the tumors is not well established There is an undeniable implication, however, that tuberculosis, among other scar producing factors, may excite the formation of some pulmonary carcinomas

The present study may be divided into several parts (1) tuberculin studies of comparable groups with concomitant radiologic search for evidence of tuberculous lesions, (2) pathologic studies of the surgically resected tumors in the carcinoma tuberculin test group, and finally (3) pathologic studies of an ancillary and unrelated group of surgically resected pulmonary carcinomas

I TUBERCULIN STUDIES

Methods—One hundred consecutive case histories of bronchogenic carcinoma were reviewed in which the tuberculin skin tests had been reported on the clinical record Included in the data collected for each patient were the age, sex, smoking habit, past history of tuberculous contact or infection, and the histologic type of carcinoma and its operability The tumors were divided into the usual four groups epidermoid (including differentiated and undifferentiated forms), adenocarcinoma, anaplastic, and bronchiolar carcinoma The diagnoses were made on resected tissue, node or tumor biopsies, or cytologic examination of the sputum

Tuberculin skin tests, using purified protein derivative (PPD),* were given to one hundred males in the same general age groups as those with bronchogenic carcinoma This control group consisted of in patients on the surgical service of New Haven Hospital, and no note was made of the specific diagnosis in each case No patient, however, had active tuberculosis or known bronchogenic carcinoma at the time of testing Injections were made intracutaneously on the flexor surface of the forearms, using 0 00002 mg Reference PPD as the first strength Second strength dosage (0 005 mg Reference PPD) was administered when the first strength elicited no reaction The reaction was classified as positive when there was one centimeter or more induration and erythema at the site of injection The smoking history was based only on whether or not the patient had smoked cigarettes rather than the degree of smoking Positive tuberculosis histories were based on proved infection and not "pleurisy," "consumption," and the like

TABLE I

	CANCER GROUP (%)	CONTROL GROUP (%)
Positive PPD	95	80
Previous known contact with tuberculosis	20	11
Previous clinical tuberculous infection	2	3
Cigarette smokers	86	77

Results—Ninety five per cent of the carcinoma group had positive tuberculin reactions as opposed to 80 per cent of the control There was a greater correlation between bronchogenic carcinoma and the positive tuberculin reaction than with cigarette smoking. Eighty-six per cent of the carcinoma group and 77 per cent of the control group were smokers (Table I). For statistical analysis of the tuberculin reactions in both groups, the chi square test was applied. The result ($\chi = 10.29$) demonstrated significance well beyond the 0.01 level; this result would be obtained by chance much less frequently than one time in a hundred ($p < 0.01$).

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*Parke Davis & Co Detroit Mich

The control and carcinoma groups had similar decade distributions (Table II). The mean ages were essentially identical: 60.7 years for the control, and 60.1 years for the carcinoma groups. The number of negative reactors in each decade in the control group was fairly constant (Table III). The 5 cases in the carcinoma group with negative tuberculin skin tests were composed of the following: 2 were in the eighth decade,[35, 36] and 2 in the sixth decade without contact histories of tuberculosis. The final case was in the fifth decade and had an extensive family and contact history of tuberculosis. All but one were cigarette smokers. It should be noted that testing in the carcinoma group was done by various contemporary, unselected members of the house staff at this hospital rather than by a single individual as in the control group. The error in observation in the carcinoma group, if any, showed favor for a higher number of negative reactors since Ghon complexes were demonstrable radiologically in 2 of the 5 patients who had negative tuberculin skin tests (see Section II).

TABLE II. TUBERCULIN SKIN TEST

DECADE	NUMBER OF PATIENTS	
	CARCINOMA GROUP	CONTROL GROUP
3-4	3	4
4-5	10	13
5-6	30	30
6-7	36	45
7-8	21	8
Totals	100	100

TABLE III. TUBERCULIN TESTS (CONTROL GROUP)
DISTRIBUTION OF NEGATIVE REACTORS

DECADE	NUMBER OF NEGATIVE REACTORS
4-5	2
5-6	5
6-7	7
7-8	6

Of the carcinoma group there were 50 epidermoid, 24 anaplastic, 15 adeno-, and 2 bronchiolar carcinomas. Nine had no definite tissue type diagnosis; 7 of these were inoperable and 2 had negative biopsies on exploration. The subsequent lethal course, however, favored the diagnosis of bronchogenic carcinoma.

II. RADIOLOGIC STUDIES

Having found that 95 per cent of patients with bronchogenic carcinoma had had a previous tuberculous infection as demonstrated by the positive tuberculin skin test, an attempt was made to determine if there was anatomic and radiologic association between tumor and tuberculous focus. Association was defined as positive when both lesions occupied the same pulmonary segment, or when a hilar tumor had adjacent tuberculous lymph nodes. The study was carried out on the above 100 cases of bronchogenic carcinoma, and involved a topographical classification of the tuberculous lesions and tumors according to pulmonary segments.

Methods.—Chest films were available in all the carcinoma-tuberculin test group. In most instances, these included planigrams as well as standard projections. Primary tuberculous foci were defined as isolated or multiple areas of discrete calcification in the lung fields, with or without hilar calcification. The latter when seen alone was considered part of the primary complex. It was realized that the differentiation between calcified tuberculous and other granulomatous foci is impossible on radiologic grounds. Secondary tuberculous infection was identified as unilateral or bilateral, fibrous or fibrocalcific densities localized to the upper lung fields, under the supposition that 90 per cent of reinfection tuberculosis occurs in the apices. It was appreciated that other nontuberculous pneumonic processes may have residual apical fibrosis in isolated instances.

An attempt was made on the basis of the x-ray studies to place the tumors in the usual ten pulmonary segments or the major bronchi. In tabulating the results, the lingula was considered as the left middle lobe. Some difficulty was encountered in the placement of large neoplasms involving the entire upper lobes. These were classified as "upper lobe unspecified." No similar difficulty was noted with middle or lower lobe tumors.

Results.—Primary tuberculous foci were seen radiologically in 47 per cent of the series. Two of the 5 patients with negative tuberculin tests had well-defined primary foci, and 2 others had "questionable primaries." In only one was there no suggestion of a primary lesion. The results of these 5 cases were not included in the 47 per cent incidence of primary foci, since the negative tuberculin reaction suggests that these foci might be other granulomata. Included in the group, however, were 2 cases of disseminated foci (Table IV).

TABLE IV. RADIOLOGIC LOCALIZATION OF CALCIFIED PRIMARY TUBERCULOUS FOCI IN 100 CASES OF BRONCHOGENIC CARCINOMA

Complete complexes	7
Incomplete complexes	38
Disseminated complexes	2
Total	47

Complete Ghon complexes were seen in only 7 cases, hilar calcification alone in 23 cases, and parenchymal foci without demonstrable hilar components in 15 cases. Thus, incomplete complexes were seen in 38 of the 100 cases, and parenchymal foci visualized in 22 of the group.

The segmental distribution of the *parenchymal* foci is seen in Table V. Segments were involved with equal frequency, and the higher number in the apical lower lobe segments is probably not significant. The upper lobe segments were involved in only 4 cases, amounting to 18 per cent of the 22 cases. This contrasts markedly with the incidence of neoplasms in the upper lobes, which is discussed in the following section.

TABLE V. CALCIFIED PRIMARY TUBERCULOUS FOCI
SEGMENTAL LOCALIZATION IN 45 CASES

SIDE	HILAR ONLY	B^1	B^2	B^3	B^4	B^5	B^6	B^7	B^8	B^9	B^{10}
Right	12	1	1	1	3	0	3	0	0	0	3
Left	11	1	0	0	0	1	4	2	0	2	0
Totals	23	2	1	1	3	1	7	2	0	2	3

In 15 of the 100 cases there was definite radiologic evidence of re-infection tuberculosis, all in the upper lobes. In an additional 3 cases, there was questionable tuberculous re-infection, and these are not included in the data for this group (Table VI). There were 13 cases of tuberculosis in the right upper lobe, and 2 in the left upper lobe. Forty-seven per cent of the 15 tumors in this group were in the apical upper lobe segments. Two tumors (13.3 per cent) were in the superior lower lobe segments. All of these patients had positive tuberculin reactions, and there were 7 epidermoid, 6 anaplastic, and one adenocarcinoma. One patient had no positive tissue diagnosis of cancer. All but one were cigarette smokers, and only one had a contact history of tuberculosis. During hospitalization, 2 patients had acid-fast bacteria seen on smear, and in 4 no sputum examinations were carried out. One patient, not included in the 15, had a positive sputum culture for tubercle bacilli but no demonstrable lesion radiologically.

TABLE VI. RE-INFECTION TUBERCULOSIS
RADIOLOGIC DIAGNOSIS IN 15 CASES

	TUMOR LOCATION			
	B^1	B^2	B^3	B^6
Numbers	7	3	0	2
Per cent of group	47.0	20.0		13.3

In only 10 of the 100 cases could an anatomic-radiologic association of tumor and tuberculous lesion be established. No parenchymal primary foci were noted in the tumor segments, but there were 7 instances of tumors adjacent to calcified nodes. Three of the patients with re-infection tuberculosis had anatomic association of tumor and tuberculous foci, and Table VII summarizes those findings. There was the tendency not to identify primary and re-infection lesions in the tumor segments. It was assumed that distal infiltrates, or dense, discrete foci, most likely represented tumor itself or distal parenchymal changes secondary to neoplastic obstruction.

TABLE VII. RADIOLOGIC LOCATION OF TUMOR AND RE-INFECTION TUBERCULOSIS IN 15 CASES

3 (20%)	In the same segment
4 (26.7%)	In the same lobe
10 (66.7%)	In the same or contralateral upper lobe

III PATHOLOGIC STUDIES OF THE RESECTED SPECIMENS IN THE CARCINOMA-TUBERCULIN TEST GROUP

Thirty-eight cases in the 100 comprising the carcinoma-tuberculin test group were subjected to the removal of a lobe or lung Of these, 33 specimens were still available for study A careful inspection was carried out to determine evidence for tuberculosis, beyond that revealed in the roentgenograms, and to evaluate the radiologic segmental localization of the tumors It was noted that the radiologic placement was incorrect in one third of the 33 cases In an attempt to establish a more accurate topographical classification, 142 additional and unrelated, surgically resected, pulmonary carcinoma specimens were examined for tumor location

Methods—The segmental location of all previously resected tumors was a relatively easy matter since it has been routine in the Department of Pathology to section all lungs along the bronchial planes In this technique, all the bronchi, including the one involved by tumor, are exposed meticulously In the present study, difficulty in segmental placement was encountered only with some hilar tumors presenting a distal extension In many cases, neoplasms apparently taking origin in the periphery had stalk-like projections to the hilar structures It was considered reasonable to assume that these involved the major bronchi only secondarily[39] Hilar tumors without larger peripheral components were considered primary in the involved bronchus The limitation of this approach is appreciated

The 33 resected specimens in the original carcinoma-tuberculin test group were studied for evidence of coexistent tuberculous infection This was done without further damage to the specimens which, on account of previous sectioning, consisted of approximately one half the original tissue mass Microscopic examination of subpleural nodules, calcified hilar nodes, apical scars, and suspicious regions, adjacent to the tumors, was carried out when indicated by gross examination Actually, only one third of the specimens had grossly demonstrable lesions warranting microscopic section It was understood well that tuberculosis is a bacteriologic diagnosis, and that hyalinized scars and calcified nodules or nodes are only presumptively tuberculous Apical scars and calcifications were not considered tuberculous, per se[33]

Results—The pathologic re-examination of these 33 specimens from the carcinoma-tuberculin test group gave additional tuberculosis data beyond that accumulated by radiography In 8 cases 9 types of lesions, not established by roentgen ray, were discovered, these are listed in Table VIII Most interesting was the finding of 2 additional instances of reinfection tuberculosis associated with the tumors Both patients had had reinfection tuberculosis diagnosed radiologically but on the side opposite from the tumor Another patient had had a peripheral, hyalinized scar related to the tumor, and a final one had had a calcified node associated with a hilar tumor Adding these 4 cases of pathologically associated tuberculosis and carcinoma to the 10 diagnosed radiologically brings the total to 14 per cent for the entire 100 cases

TABLE VIII. ADDITIONAL TUBERCULOSIS FINDINGS ON ANATOMIC STUDY IN 33 CASES OF RESECTION

	OCCURRENCE
Apical calcification	1
Multiple calcified foci	1
Calcified node associated with tumor	1
Hyalinized scar associated with tumor	1
Several hyalinized foci	1
Re-infection tuberculosis in additional segments	2
Tumors associated with re-infection tuberculosis	2

Since anatomic placement of the tumors appeared to be more accurate than radiologic placement alone, the 33 resected tumors were supplemented by 142 unrelated carcinoma specimens, totaling 175, for anatomic study. These are compared with the remaining 67 nonresected tumors in the x-ray studies of the original carcinoma-tuberculin test group in Table IX. There was fairly close agreement with the exception that fewer tumors were considered primary in the major bronchi on gross examination. Twenty-one per cent of the neoplasms were primary in the hilar and lobar bronchi, and 79 per cent had obvious segmental or subsegmental origin. The predilection of bronchogenic carcinoma for particular regions contrasts with the apparent haphazard distribution of the primary parenchymal tuberculous focus as noted in the previous section, and summarized in Table V.

TABLE IX. BRONCHOGENIC CARCINOMA

CASES	ULB	B^1	B^2	B^3	UL UNSPEC.	B^4	B^5	RIB
				Segmental Location				
67 (x-ray)								
Right side	2	5	3	6	3	0	1	3
Left side	2	4	6	5	3	1	2	—
(Per cent)	(6)	(13.5)	(13.5)	(16.3)	(9.0)	(1.5)	(4.5)	(4.5)
175 (gross)								
Right side	3	21	15	17	1	2	2	7
Left side	7	9	19	13	1	2	2	—
(Per cent)	(5.7)	(17.2)	(19.4)	(17.2)	(1.1)	(2.3)	(2.3)	(4.0)
Totals								
242	14	39	43	41	8	5	7	10
(Per cent)	(5.8)	(16.1)	(17.8)	(16.9)	(3.3)	(2.1)	(2.8)	(4.1)

CASES	MSB	LLB	B^6	B^7	B^8	B^9	B^{10}
			Segmental Location				
67 (x-ray)							
Right side	3	3	0	0	0	0	0
Left side	2	7	5	0	0	0	1
(Per cent)	(7.5)	(15.0)	(7.5)	(0)	(0)	(0)	(1.5)
175 (gross)							
Right side	1	5	17	5	1	1	2
Left side	0	6	7	1	1	2	5
(Per cent)	(0.6)	(6.3)	(13.7)	(3.4)	(1.1)	(1.7)	(4.0)
Totals							
242	6	21	29	6	2	3	8
(Per cent)	(2.5)	(8.7)	(12.0)	(2.5)	(0.8)	(1.3)	(3.3)

Legend: MSB = main-stem bronchus; RIB = intermediate bronchus; ULB = upper lobar bronchus; LLB = lower lobar bronchus.

The variance of segmental placement by gross dissection as compared with radiologic means for the 33 resected cases is summarized in Table X. In view of the discrepancy noted, roentgen analysis of the tumor site was carried out again. Films of 10 of the 12 patients cited were available for re-evaluation. In 2 cases it was found that more exact localization could have been made from information present in the films. The roentgen localization remained unchanged in 5 cases, the exact position of the tumor being masked by associated atelectasis or pneumonitis. This was particularly true where a tumor arose in a proximal segmental region close to the hilum. As indicated in other studies,[10] the clinical manifestations of the tumor which brought the patient to x-ray examination were not present until a lobar bronchus or the right intermediate bronchus (see Case 3, Part II, Table X) had been encroached upon. When this occurs, definition of the origin of the tumor is extremely difficult or impossible. In the remaining 3 cases it was felt that the localization had been made with insufficient radiographic studies.

TABLE X. VARIATIONS IN X-RAY AND GROSS TUMOR PLACEMENT IN 33 CASES

I. 4 Cases Segmental		
	X-Ray	*Gross*
	B^2	B^3
	B^{10}	B^6
	B^9	B^7
	B^3	B^1
II. 6 Cases Hilar and Lobar		
	X-Ray	*Gross*
	ULB	B^3
	ULB	B^2
	RIB	B^6
	LLB	B^3
	LLB	B^6
	MSB	ULB
III. 2 Cases Upper Lobe Unspecified		
	X-Ray	*Gross*
	Unspec.	ULB
	Unspec.	B^3

IV. PATHOLOGIC STUDY OF 50 UNRELATED SURGICALLY RESECTED BRONCHOGENIC CARCINOMAS

Finally a macro- and micropathologic study of 50 additional resected specimens, not in the carcinoma-tuberculin test group, was undertaken to investigate further the incidence of associated pulmonary tuberculosis and bronchogenic carcinoma.

Methods.—This examination was carried out in similar fashion to the previous pathologic studies, and histologic sections were taken only when indicated on gross examination. Sectioning was done carefully in such a way as to preserve the specimens, which again consisted of only one half the original tissue mass.

Results.—Five types of tuberculous lesions were found in 25 cases. The remaining 25 did not appear to warrant microscopic sectioning. In the latter group, approximately one half were hilar or lobar bronchial tumors, and most of the adjacent lymph nodes had been extirpated previously. Table XI lists

TABLE VIII. ADDITIONAL TUBERCULOSIS FINDINGS ON ANATOMIC STUDY IN 33 CASES OF RESECTION

	OCCURRENCE
Apical calcification	1
Multiple calcified foci	1
Calcified node associated with tumor	1
Hyalinized scar associated with tumor	1
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Re-infection tuberculosis in additional segments	2
Tumors associated with re-infection tuberculosis	2

Since anatomic placement of the tumors appeared to be more accurate than radiologic placement alone, the 33 resected tumors were supplemented by 142 unrelated carcinoma specimens, totaling 175, for anatomic study. These are compared with the remaining 67 nonresected tumors in the x-ray studies of the original carcinoma-tuberculin test group in Table IX. There was fairly close agreement with the exception that fewer tumors were considered primary in the major bronchi on gross examination. Twenty-one per cent of the neoplasms were primary in the hilar and lobar bronchi, and 79 per cent had obvious segmental or subsegmental origin. The predilection of bronchogenic carcinoma for particular regions contrasts with the apparent haphazard distribution of the primary parenchymal tuberculous focus as noted in the previous section, and summarized in Table V.

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				Segmental Location				
67 (x-ray)								
Right side	2	5	3	6	3	0	1	3
Left side	2	4	6	5	3	1	2	—
(Per cent)	(6)	(13.5)	(13.5)	(16.3)	(9.0)	(1.5)	(4.5)	(4.5)
175 (gross)								
Right side	3	21	15	17	1	2	2	7
Left side	7	9	19	13	1	2	2	—
(Per cent)	(5.7)	(17.2)	(19.4)	(17.2)	(1.1)	(2.3)	(2.3)	(4.0)
Totals								
242	14	39	43	41	8	5	7	10
(Per cent)	(5.8)	(16.1)	(17.8)	(16.9)	(3.3)	(2.1)	(2.8)	(4

CASES	MSB	LLB	B^6	B^7	B^8	B^9
			Segmental Location			
67 (x-ray)						
Right side	3	3	0	0	0	0
Left side	2	7	5	0	0	
(Per cent)	(7.5)	(15.0)	(7.5)	(0)	(0)	
175 (gross)						
Right side	1	5	17	5		
Left side	0	6	7	1		
(Per cent)	(0.6)	(6.3)	(13.7			
Totals						
242	6	21	29			
(Per cent)	(2.5)	(8.7)	(12.0)	(2.		

Legend: MSB = main-stem bronchus; RIB = intermed
lobar bronchus; LLB = lower lobar bronchus.

The variance of segmental placement by gross dissectio
radiologic means for the 33 resected cases is summarized in T

may have a variety of etiologic agents Recent studies of "lung scar cancers" seem to support the theory that it is the scar, and only remotely the agent causing the scar, that is important in the pathogenesis of the disease Tuberculosis is a common cause of pulmonary scars The most frequent location of bronchogenic carcinoma in the upper lobes and the apical segment of the lower lobes suggests a relationship to *re infection* tuberculosis Against this, however, are the facts that (1) only 15 per cent of the cases in the carcinoma tuberculin test group had demonstrated coexistent re infection tuberculosis, (2) only one half of these had a positive anatomic association of both diseases, and (3) that the anterior upper lobe segment (B^2), which was a common site of carcinoma, was less commonly the seat of re infection tuberculosis

The haphazard distribution of the primary parenchymal tuberculous focus is not characteristic of bronchogenic carcinoma Furthermore, 22 per cent of the 95 patients with bronchogenic carcinoma with positive tuberculin skin tests had primary parenchymal foci radiologically separate from the tumor mass Considering such tumors to be caused by a healed focus would imply that more than one focus existed Medlar[33] has emphasized that multiple (two or more) primaries occur in only 10 per cent of lungs which are the site of primary tuberculous infection, and this makes the theory of multiple primaries in cases of bronchogenic carcinoma less likely There was no instance of radiologically positive anatomic association of primary *parenchymal* tuberculous lesion and tumor in the 100 cases studied radiologically This was due partly to our reluctance to classify a dense focus near or within a tumor shadow as tuberculous In addition, in 78 of the 95 tuberculin *positive* cases no parenchymal component of the primary tuberculous complex could be detected radiologically Rich[38] has stressed that x ray studies are notoriously poor in demonstrating these minute lesions The high incidence of nonvisualization may indicate that the tuberculous foci were in fact within the tumor mass The difficulty in finding these foci on gross examination of a large, solid tumor is obvious, and one must remember that they might be destroyed by malignant growth Particles of calcium seen on microscopic examination of tumors not uncommonly occur as the result of local necrosis, and cannot be interpreted as remnants of tuberculous disease Attempts to study tumors by serial sections were not carried out in the study

The incidence of positive reactors in the control group correlates closely with the findings of other investigators dealing with mass surveys of eastern metropolitan areas[34] The tuberculin skin test might be of greater value in areas where the positive reaction is less common than in the East In this instance, a 95 per cent incidence of positive reactors in cases of bronchogenic carcinoma would be of even greater statistical significance

SUMMARY

1 One hundred cases of bronchogenic carcinoma were compared with a control group with respect to the tuberculin skin reaction Ninety five per cent of those with carcinoma were tuberculin positive as compared to 80 per cent in the control group This difference has statistical significance in the order $p<0\ 01$

2. Primary tuberculous calcified foci were seen radiologically in 47 per cent of the 100 cases. In only 7 per cent of these were complete Ghon complexes seen. The parenchymal component was visualized in 22 per cent of cases, and had a random distribution as regards pulmonary segments.

3. Re-infection tuberculosis was noted radiologically in 15 per cent of the bronchogenic carcinomas studied.

4. Positive anatomic association was defined as (a) their co-situation in the same segment, or (b) the approximation of tumor and a calcified hilar node. On radiologic and gross examination, this was noted in 14 per cent of the 100 cases studied.

5. The segmental distribution of bronchogenic carcinoma was tabulated on radiologic examination of 67 of the 100 cases, on gross examination of 33 resected specimens of the same series, and 142 unrelated, additional specimens. The predilection of tumors for the upper lobe and superior lower lobe segments was noted. The upper lobe segments were all involved, and with equal frequency.

6. Segmental placement of tumors by radiologic means may be misleading with certain peripheral neoplasms having extensions to major bronchi. In such instances, associated atelectasis and pneumonitis may mask the actual position of the tumor.

7. The possible relationship of bronchogenic carcinoma to antecedent tuberculosis is discussed with particular reference to the primary and re-infection types of lesions.

8. The shortcomings of a purely statistical approach to tumor pathogenesis is well demonstrated.

ADDENDUM

Since this study has been compiled, an additional 28 consecutive patients with pulmonary carcinoma, admitted to the Thoracic Surgical Service, have been subjected to the tuberculin skin test. In every case the reaction was positive, using the same criteria stated in Part I of this report.

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LEIOMYOMA OF INTERMEDIATE BRONCHIAL ORIGIN

A Case Report

S. W. Berkheiser, M.D., and J. T. Szypulski, M.D., Harrisburg, Pa.

BENIGN mesodermal tumors originating from intermediate bronchi are extremely rare. Most lesions of this type originate in main-stem bronchi. According to Liebow,[1] fibromas and chondromas are the most frequent tumors, accounting for from 80 to 90 per cent of benign intrabronchial tumors. In 1955, Hirose and Hennigar[2] reported only the third case of intrabronchial leiomyoma, and extensively summarized the literature. Because of the rarity, the following case is reported.

CASE REPORT

A 43-year-old white housewife was admitted to the hospital on Dec. 9, 1958. Five months previously she had developed an upper respiratory infection. Following the infection she noted a persistent cough, which was productive of thick, yellowish mucus. She also complained of intermittent pain over the right chest, which was aggravated by deep inspiration. The past medical history was unremarkable, and no previous operations had been performed.

Physical examination disclosed a temperature of 99° F., pulse rate of 80, respiration rate of 20, and blood pressure of 140/90 mm. Hg. Slight dullness and absent breath sounds over the right lung base were the only significant physical findings.

Laboratory studies, including red and white cell count, hemoglobin determination, and urinalysis, were in the normal range. An electrocardiogram was interpreted as within normal limits.

Roentgenogram of the chest disclosed a right pleural effusion, partial atelectasis of the right middle and lower lobes, and definite elevation of the right leaf of the diaphragm.

On the second hospital day, bronchoscopy was performed by one of us (J. T. S.). A rounded smooth mass was observed projecting into the lumen of the right intermediate bronchus, approximately 1 cm. below the inferior spur of the right upper lobe. The lesion produced virtually complete obstruction of the right middle and lower lobe bronchi. The mass was biopsied and partially resected.

Histologic examination revealed a benign leiomyoma. The patient was discharged on the fourth hospital day to be readmitted at a later date for further definitive therapy.

She was readmitted to the hospital one month later. Her clinical condition had remained unaltered. The chronic cough persisted and had not changed in character. Physical findings at this time again revealed dullness and absent breath sounds over the right lung base. A few moist râles, and an inspiratory wheeze were audible over the right upper posterior lung field. Laboratory data and chest roentgenogram were unchanged. Preoperatively the patient received streptomycin and penicillin therapy.

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Received for publication March 11, 1959.

[illegible]

[illegible] was [illegible] There was [illegible] Because of [illegible]

The post-operative c[illegible] the patient was [illegible]

Pathology—Grossly [illegible] lobes with a total weight [illegible] and measured. D[illegible] a polypoid tumor, 1.2 cm [illegible] surface was smooth, [illegible] had produced complete [illegible]

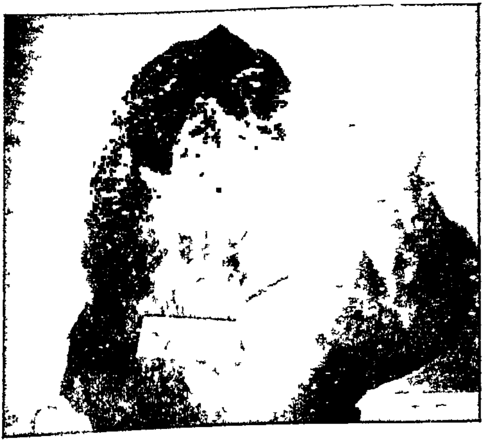


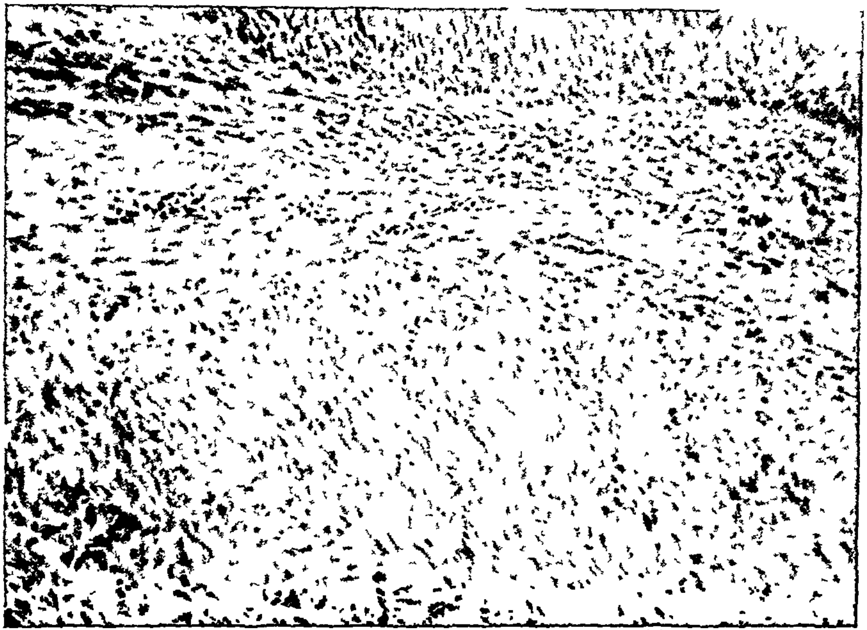
Fig 1 Gross photograph showing polypoid intrabronchial tumor

lobes were markedly dilated down to the terminal portions The mucosa was roughened, granular, and contained purulent gray yellow exudate The adjacent lung parenchyma showed extensive pneumonitis of obstructive type The hilar lymph nodes were moderately enlarged

Microscopic examination Sections of the bronchoscopic specimen, and the lesion from the lobectomy showed an identical structure The tumor was observed to originate just beneath the submucosa of the bronchus A thin, but definite fibrous capsule was present (Fig 2) Slight squamous metaplasia was noted in the overlying bronchial mucosa The neoplasm was composed of elongated spindle shaped cells, which appeared to represent a mixture of smooth muscle and fibroblastic types In some regions, definite palisading of nuclei was observed Individual nuclei were fairly uniform and regular, and excessive mitotic activity was not present (Fig 3) Specific stains by the and trichrome methods demonstrated that the predom cells type A sparse fibrous or collagenous component pattern was consistent with a benign leiomyoma of b

Sections of lung parenchyma confirmed the impression of chronic interstitial pneumonitis of obstructive type, and also showed extensive bronchiectasis. The hilar lymph nodes showed only anthracotic pigmentation.

Fig. 2.



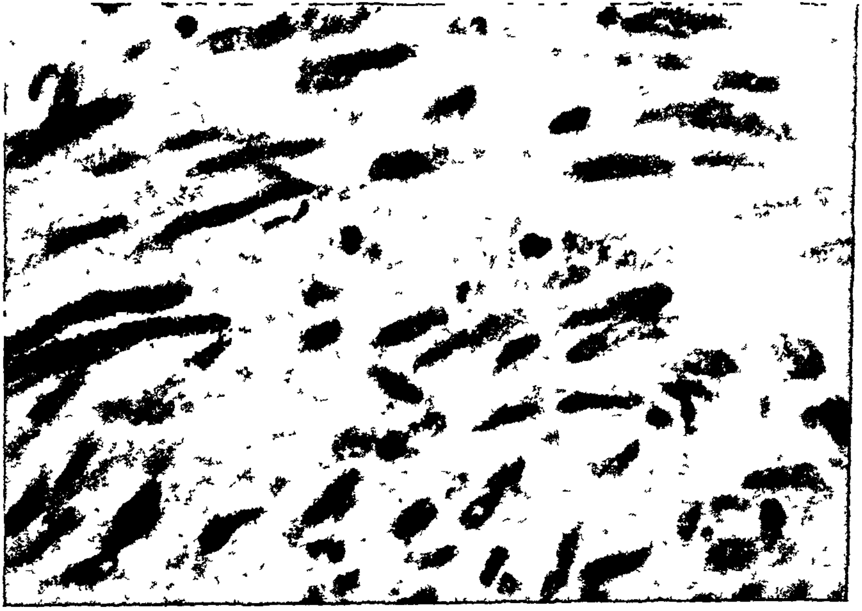


Fig. 3.

Fig 2—Photomicrograph showing the origin of leiomyoma in submucosal zone of the bronchus (×160).

Fig 3—Higher power photomicrograph showing details of cell morphology (×320).

DISCUSSION

There is no doubt that the present case is representative of benign intrabronchial leiomyoma. There was no evidence of parenchymal origin. The location and histologic features preclude a metastatic lesion. Hamartomas may occasionally contain large elements of smooth muscle, but admixtures of other mesodermal components aid in the diagnosis.

Other types of intrabronchial tumors have been described. Liebow[1] states that lipomas, lymphoma, myoblastoma, and even a plasmocytoma have been recorded. Primary leiomyosarcoma may occur, but is likewise extremely rare.[3] The cellular morphology of the present case was not typical of leiomyosarcoma, although differentiation is not always made with ease.

The histologic features of the present case are very similar to the case described by Hirose and Henniger.[2] The latter authors were able to find only 2 previous cases of intrabronchial leiomyoma, although six instances of parenchymal origin were found. The principal features which were of aid in the differentiation of leiomyoma from other more common bronchial tumors was adequately discussed.

Clinically, it is apparent that the symptoms of bronchial leiomyoma may resemble those of bronchial adenoma. Pneumonitis of obstructive type is common to both lesions, and is directly responsible for many of the clinical symptoms. If prolonged bronchial obstruction continues without surgical intervention, bronchiectasis may follow as a secondary complication.

The treatment of bronchial leiomyoma will vary according to factors affecting the individual case. The site of origin, malignant potentialities of the neoplasms, the presence of secondary complications, such as bronchiectasis or extensive pneumonitis, are factors which must be considered. If the tumor is confined to a small focus, adequate wide resection would be appropriate. In the presence of extensive bronchiectasis and pneumonitis, however, lobectomy may be necessary. On the basis of histology, irradiation therapy could be expected to offer no possible benefits.

SUMMARY

A rare case of leiomyoma of intermediate bronchial origin is presented and discussed.

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PRESCALENE FAT PAD BIOPSY

Analysis of 362 Cases

*George A. Higgins, M.D., and William E. Brownlee, M.D.,**
Kansas City, Kans., and Kansas City, Mo.

Although frequent involvement of the supraclavicular lymph nodes by metastatic carcinoma of the stomach has been a well-documented clinical observation since the time of Virchow, it has been only during the past decade that the prescalene fat pads with their abundance of lymphoid tissue have been studied as a reflection of various pulmonary diseases. Since Daniels'[5] presentation, in 1949, of prescalene fat pad biopsy as a method of diagnosing certain intrathoracic diseases, several series of cases have been presented with statistical analysis of the value of this procedure as a supplemental diagnostic tool in the study of pulmonary disease.[1, 4, 10, 12] Various modifications and extensions of the simple prescalene fat pad removal have been suggested, and the lymphatic drainage of the lungs has been restudied in an effort to improve the value of this procedure as a diagnostic and prognostic procedure.[7]

In general, removal of the prescalene fat pads has been useful for two different purposes. The procedure has been used as a diagnostic aid in bronchogenic carcinoma as well as other pulmonary diseases when the conventional diagnostic methods fail to establish clearly a diagnosis. In addition, it has been used as a criterion of operability in cases of bronchogenic carcinoma, it being the opinion of most thoracic surgeons that involvement of the prescalene lymph nodes by metastatic carcinoma constitutes a contraindication to excisional surgery in most instances. Although there has been general agreement that biopsy of palpable supraclavicular nodes should be done, removal of the prescalene fat pad with its contained nodes in the absence of clinically palpable enlargement has continued to be the subject of controversy. In an effort to evaluate the diagnostic and prognostic value of this procedure, we have reviewed the experiences during the past 5 years (January, 1953-December, 1957), at the Kansas City Veterans Administration Hospital and

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*During the time that this work was done, Dr. Brownlee was a Fellow of the American Cancer Society and his portion of work described in this paper was done under an American Cancer Society Clinical Fellowship. Dr. Brownlee's present address is 1616 North Norton, Tucson, Arizona.

the University of Kansas Medical Center, which comprises 362 consecutive prescalene node biopsies. The combined experience has been compiled and tabulated and the experience of each hospital tabulated separately for comparative purposes.

For the most part, the procedures were done by the resident staff, often by the first or second year resident, and the technique employed (Fig. 1) consisted of simple removal of the prescalene fat pad under local anesthesia

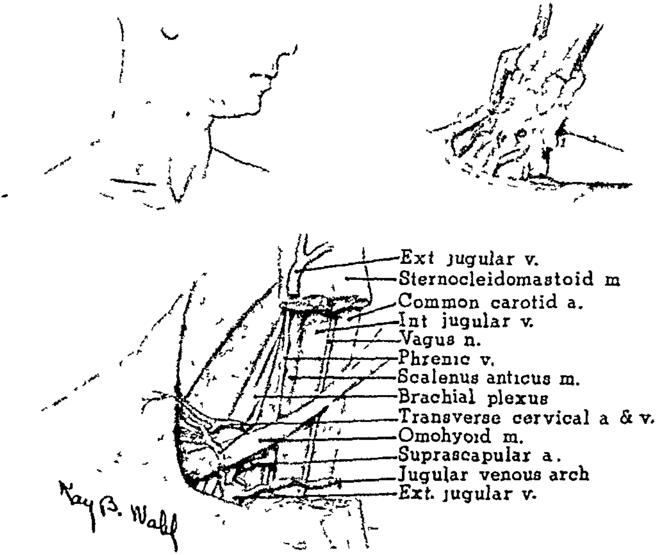

Fig 1—Drawing to illustrate the anatomic features of the supraclavicular triangle as well as the skin incision and removal of the prescalene fat pad

In almost all instances, the right fat pad was removed when the right lung was involved and the left fat pad removed when the left lung was involved Although many authors[2, 6, 9] have recommended removal of the right scalene nodes for pulmonary lesions involving the left lower lung field, based upon the lymphatic drainage patterns reported by Rouviere,[8] we have continued to remove the ipsilateral node. Serious doubt of this concept of cross drainage of the lymphatics from the left lower lobe has been raised by the recent work of Correll and Langston[3] who found an essentially ipsilateral drainage pattern by injecting dye into various areas of the dog's lung by a transbronchial

route. Likewise, the results reported by Shields, Lees, and Fox[11] of 12 per cent histologically positive nodes in their series of biopsies of nonpalpable nodes, in which bilateral fat pad removal was done in lung lesions involving the middle or lower lung field on the left side, is almost identical with the results in our study (12.7 per cent). Removal of the opposite fat pad, therefore, may be indicated when the primary lung lesion is in the left lower lobe or hilum and the ipsilateral nodes are histologically negative.

Table I contains the summary of the entire experience of the two institutions comprising 362 biopsies, of which 98 or 27 per cent were diagnostically positive; 68 or 19 per cent were positive for carcinoma, while the remaining 30 or 8 per cent were diagnostically positive for conditions other than carcinoma. Comparison of the total positive results obtained in the Veterans group and the University group shows a considerable discrepancy—21 per cent versus 37 per cent. The reason for this is readily apparent in Table II which shows the much higher percentage of clinically palpable nodes in the University group than in the Veterans group—44 per cent versus 23 per cent. During the period of time when these figures have been accumulated, the use of scalene node biopsy as a diagnostic screening test has been used much more freely by the Veterans Administration staff than by the University group.

TABLE I. TABULATION OF THE ENTIRE SERIES OF BIOPSIES WITH THE NUMBER AND PERCENTAGE WHICH WERE POSITIVE ON HISTOLOGIC EXAMINATION

	V.A.	K.U.	TOTAL
Total biopsies	224	138	362
Positive–cancer	35 (16%)	33 (24%)	68 (19%)
Positive–other than cancer	12 (5%)	18 (13%)	30 (8%)
Total positive biopsies	47 (21%)	51 (37%)	98 (27%)

TABLE II. SUMMARY OF PALPABLE AND NONPALPABLE NODES IN THE SERIES

	V.A.	K.U.	TOTAL
Total biopsies	224	138	362
Clinically palpable node	52 (23%)	60 (44%)	112 (30%)
No clinically palpable node	172 (77%)	78 (56%)	250 (69%)

Table III contains a breakdown of the findings in those patients who had a scalene biopsy done with a final diagnosis of bronchogenic carcinoma made by biopsy, operation, or autopsy. Of the 208 patient with bronchogenic carcinoma, 68, or one third, had metastatic involvement of the scalene nodes. Comparison of the findings in the two institutions again shows a fairly wide discrepancy, reflecting the fact that prescalene fat pad biopsy in the presence of nonpalpable nodes was done with much greater frequency in the Veterans Hospital group than in the University group. Even so, there were 18 instances in the total study in which the scalene nodes were involved by metastatic carcinoma in which no palpable enlargement of the nodes was present.

TABLE III. COMPILATION OF THE FINDINGS IN THE 208 PATIENTS ULTIMATELY PROVED TO HAVE CARCINOMA OF THE LUNG

	V.A.	K.U.	TOTAL
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Patients with final diagnosis of cancer	129	79	208
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No clinically palpable node	13 (10%)	5 (6%)	18 (9%)

Table IV contains an analysis of the 208 patients having a final diagnosis of bronchogenic carcinoma with respect to the presence or absence of palpable nodes and the histologic findings in the two groups. Out of the 66 patients having palpable nodes, 50 (75 per cent) were found to be histologically positive for bronchogenic carcinoma. However, in 16 instances, the enlarged nodes were histologically negative, emphasizing that the presence of enlarged prescalene nodes in the presence of bronchogenic carcinoma is not invariably indicative of metastatic involvement. The lower portion of Table IV contains the most significant figures obtained from the entire study. Of the 208 patients in the study whose final diagnosis was bronchogenic carcinoma, 142 had nonpalpable scalene nodes on clinical examination. Of this group, 18 (12.7 per cent) were found to have histologic involvement on microscopic examination. The fact that the percentages of histologically positive nodes in the two groups were almost identical—13 per cent versus 11 per cent—is doubly significant in those patients with clinically nonpalpable nodes, since the difference in the selection of patients in the two groups, as reflected by the discrepancy in figures contained in the other tables, would have no effect on the number of histologically positive specimens in those patients having nonpalpable nodes on clinical examination.

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Histologically neg cancer	10 (31%)	6 (18%)	16 (24%)
No Clinically Palpable Node	97	45	112
Histologically pos cancer	13 (13%)	5 (11%)	18 (13%)
Histologically neg. cancer	84 (87%)	40 (89%)	124 (87%)

*The 208 patients having carcinoma of the lung have been subdivided into those having clinically palpable nodes and those not having palpable nodes with a summary of the histologic findings in the two groups

Diagnoses other than bronchogenic carcinoma which were established by scalene fat pad biopsy are summarized in Table V It will be noted that in 10 of the cases in the University group the diagnosis was carcinoma originating outside the lung. In all but 3 of these patients, definite pulmonary abnormalities were present on x-ray In a recent case, done since the study

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Diagnoses other than bronchogenic carcinoma which were established by scalene fat pad biopsy are summarized in Table V. It will be noted that in 10 of the cases in the University group the diagnosis was carcinoma originating outside the lung. In all but 3 of these patients, definite pulmonary abnormalities were present on x-ray. In a recent case, done since the study was completed, scalene lymph nodes were found to contain metastases from a papillary carcinoma of the thyroid entirely unsuspected in a man having bronchogenic carcinoma resected by pneumonectomy.

TABLE V. CONDITIONS OTHER THAN CARCINOMA OF THE LUNG DIAGNOSED BY SCALENE NODE BIOPSY

	V.A.	K.U.	TOTAL
Boeck's sarcoid	3	2	5
Tuberculosis	3	1	4
Nonspecific granuloma	3		3
Lymphoma	1	3	4
Infectious mononucleosis	1		1
Thrombosed subclavian vein	1		1
Carcinoma other than lung	0	10	10

Table VI contains a breakdown of the histologic cell types found in the scalene nodes in those patients with bronchogenic carcinoma. For simplification, the lesions were divided into squamous cell carcinoma, adenocarcinoma, and undifferentiated carcinoma. The variations between the two groups of patients probably reflect a difference in the classification patterns used by the various pathologists concerned. As might be expected, there was a preponderance of undifferentiated carcinoma in the histologically positive scalene group although the number of squamous cell carcinomas and adenocarcinomas is significant.

TABLE VI. SUMMARY OF HISTOLOGIC CLASSIFICATION IN THE SCALENE FAT PADS SHOWING METASTATIC BRONCHOGENIC CARCINOMA

	V.A.	K.U.	TOTAL
Squamous cell carcinoma	7	4	11
Adenocarcinoma	9	3	12
Undifferentiated	19	26	45
Total	35	33	68

SUMMARY

The diagnostic and prognostic significance of prescalene fat pad biopsy has been determined in a study of 362 patients having this procedure during the past 5 years. The series includes 138 patients from a University Hospital and 224 patients from an associated Veterans Hospital. A comparison of the two series as well as a study of the entire group is made.

Of the 362 biopsies, 98 (27 per cent) were positive, 68 (19 per cent) for carcinoma and 30 (8 per cent) for diseases other than carcinoma.

Of the 208 patients whose final diagnosis was bronchogenic carcinoma, 68 (32 per cent) had a positive prescalene fat pad biopsy.

Of the 68 instances showing a histologic diagnosis of carcinoma, 50 (73 per cent) had clinically palpable nodes, while 18 (27 per cent) had nonpalpable nodes.

Of the 142 patients in whom the final diagnosis was bronchogenic carcinoma and who had nonpalpable nodes on clinical examination, 18 (12 per cent) were positive on histologic examination.

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AN ELECTRONICALLY CONTROLLED RESPIRATOR FOR THE EXPERIMENTAL LABORATORY

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INTRODUCTION

A RESPIRATOR, consisting of an electronic timing circuit and two solenoid valves, has been used by us in the experimental laboratory for about 7 years. For some of the earlier respirators, the electrical timing units were built by electrical technicians or by us.[3] These respirators worked well and they are still being used, but it is now much easier to build the respirator with a commercially available timer. The respirator can be assembled from a few purchased parts and some standard plumbing fittings. It will operate either on compressed air from a laboratory wall line or on gas from a tank of compressed air or oxygen.

THE APPARATUS

The apparatus is illustrated in Figs. 1 and 2. The timing unit* is a mulivibrator circuit which has been employed in various designs as a cycle timer for industrial processes. The reader will be spared description of the electronic circuits. I am not sure of the details of the circuit in this commercial apparatus but circuits of similar purpose are to be found in the nonmedical literature.[1, 2] The length of a timing cycle in these devices is determined by the length of time it takes a condenser to discharge through a variable resistor. Thus, by turning a knob to change the resistance, the length of the cycle is varied. In action, the timing circuit operates a relay so that this relay is alternately on and off. The length of the on and off cycles may be varied independently in a range from a fraction of a second up to about 12 seconds.

The power supply (150 volts AC) and the electrical solenoid valve are wired to a terminal strip built in the timing unit so that one solenoid valve

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*Repeat cycle timer Model No. 4, G. C. Wilson Co., Huntington, West Virginia.

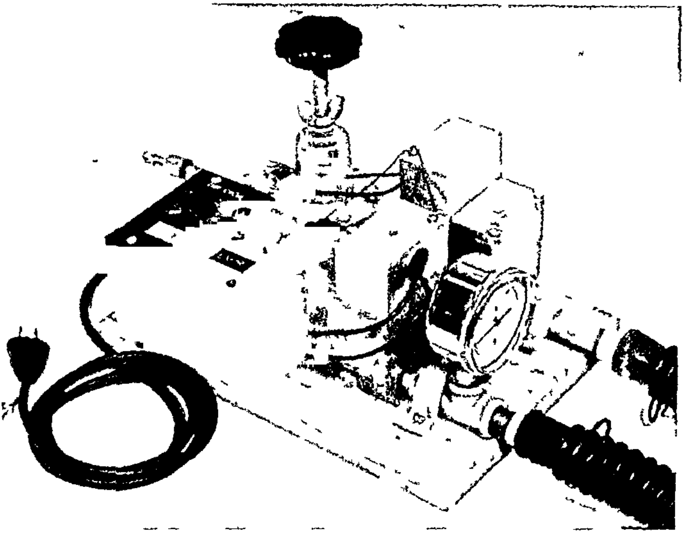

Fig 1.—Photograph of the respirator illustrating its compact assembly on a board

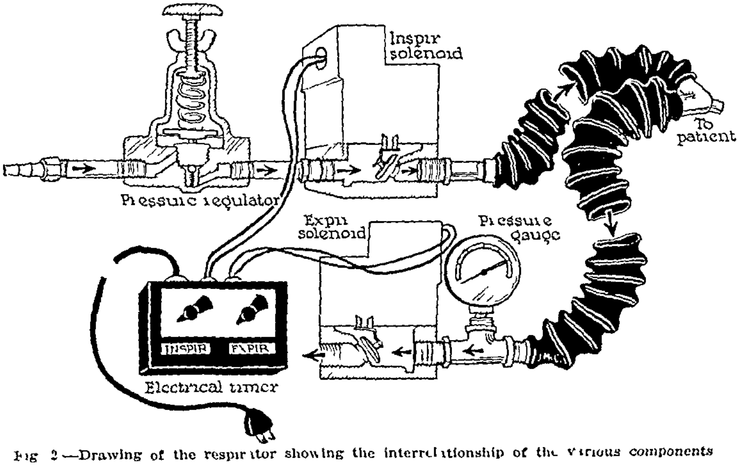

Fig 2.—Drawing of the respirator showing the interrelationship of the various components

receives current while the other valve is off and vice versa. The correct way of connecting the solenoids becomes relatively clear after a little study of the timing device. One solenoid becomes an inspiratory valve and the other the expiratory valve of the respirator. Thus, one of the controls of the timer regulates the length of inspiration and the other the length of expiration. The respiratory rate can be easily adjusted from 4 or 5 per minute up to more than 60 per minute, with a wide range of inspiratory and expiratory ratios. The solenoid valves,[*] which are identical, are normally closed and only opened when a current is applied. These valves have large apertures and rubber-cushioned flaps which make them nearly silent. If the gas pressure is too high on the inspiratory side, this type of valve will lock in the closed position. This disadvantage has not appeared with other solenoid valves we have used.[†] But these other solenoids are much noisier. The quiet operation of the Minneapolis Honeywell valve is worth the slight additional care necessary in controlling the inflow gas pressure. Gas entering the inspiratory solenoid must be under controlled pressure. If tank gas is used, a standard reducing valve attached to the tank is sufficient.[‡] This is a pressure, not a flow rate, valve. If air from a laboratory pressure line is used, there must be a pressure-reducing valve proximal to the solenoid valve. We have used the valve shown in the illustrations.[§] It is not quite as sensitive as one would like but this has been no great disadvantage. If a tank source is used with this valve in position, either it or the tank valve may be open to allow control of pressure by the other pressure regulator.

Standard pipe fittings connect the solenoids to the respirator tubing and the inspiratory solenoid to the reducing valve. The expiratory solenoid exhausts into the ambient air. Attachment of a pressure gauge[‖] is a useful refinement. It allows the operator to observe the pressure in the animal's respiratory tree. Other refinements may be added as it is desired. An on and off switch has been inserted in some of these models. It is possible to hook up the resistors so that the rate and ratio adjustments may be used rather than adjustments for the length of inspiration and expiration. Grounding of the solenoids and the timer is essential if sensitive recording equipment is to be used in the laboratory.

Earlier models of this particular respirator have been used in literally thousands of dog experiments with only occasional repair problems. The model described here is newer and thus less extensively tested but it seems to be reliable. The machine is not explosion proof.

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[*] Silent gas valve Model No. V40A, Minneapolis Honeywell Regulator Co., Minneapolis 8, Minn.

[†] Valve No. V5-D1790S, Skinner Electric Valve Division, The Skinner Chuck Co., New Britain. Conn.

[‡] Two stage cylinder regulator, Style 8401, Air Reduction Company, New York 17, N. Y.

[§] Precision pressure regulator, Type 11,400, C. A. Norgren Company, 222 Santa Fe Drive, Denver 9, Colo.

[‖] No. 6 bag pressure indicator, Ohio Chemical and Surgical Equipment Co., 1400 E. Washington Avenue, Madison 10, Wis. (The additional fittings sold with this gauge are unnecessary.)

The same basic respirator has also been used clinically, both in the operating room and on the wards. The clinical model has some additional refinements and it is still undergoing tests and alterations.

SUMMARY

An electronically controlled respirator, consisting of a cycle timer and two solenoid valves, has been described. It is easy to assemble, reliable, and flexible in operation.

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A CARDIOVASCULAR SIMULATOR FOR THE EVALUATION OF PROSTHETIC AORTIC VALVES

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I. INTRODUCTION

The cardiovascular simulator described herein is a mechanical analogue of the left ventricle, aorta, and systemic circulation. It was designed to facilitate analysis of prosthetic aortic valves, and with modifications it can be used for mitral valve analysis. Potentially, the simulator is useful as a teaching and study aid, since such characteristics as peripheral resistance, aortic distensibility, etc., can be independently varied, and the effects on ventricular and aortic dynamic pressure curves immediately observed.

The resistance of a valve to blood flow, as measured by the pressure drop across it, is a function of both instantaneous flow rate and the degree of restriction. The average ejection rate during systole is only 270 ml. per second (i.e., 60 ml. stroke output ÷ 0.22 sec. ejection period) as compared to the actual peak rate of 900 ml. per second, which is developed for a small portion of the ejection time. To evaluate accurately valve stenosis, therefore, it was mandatory that the simulator duplicate the shape of the normal ventricular ejection curve as well as total stroke volume.

In order to test reliably the ability of a prosthetic valve to withstand the hydraulic forces imposed during diastole, it was also necessary to duplicate the shape of the ventricular pressure curves as well as the absolute magnitudes. The strength of materials under fatigue stress often depends on the rate of change of stress in addition to the magnitude of stress. The aortic valve is subjected to particularly high stress rates at the instant it snaps shut and must maintain diastolic pressure against the rapidly falling left ventricular pressure.

Like any system which contains a number of interdependent variables, the simulator was most conveniently designed by fixing one variable as a basic parameter. For practical reasons, the left ventricular ejection curve was selected as the parameter from which the system was to be designed. The volume and pressure curves from Wiggers[7] were used as the standard normal curves.

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It must be noted that Wiggers' volume curve has been derived from the combined ventricular volumes The right ventricle, lungs, left ventricle, and systemic circulation are normally in series in a closed fluid system, therefore, assuming no transient changes are taking place in the various vascular volumes, the left and right total ejection volumes per heartbeat are identical However, the fluid dynamic "loads" (such as the magnitudes of resistance, distensibility, etc) imposed upon the two ventricles are greatly different Consequently, the instantaneous flow rates are different in the two pumping chambers even though the total ejection volumes are identical This results in distortion of the shape of the volume curve when the combined ventricular volume is used to plot left ventricular ejection Despite this inherent error, the ejection curve of Wiggers, being the most reliable data available, was used

Austen, Shaw, Scannell, and Thurlbeck[4] have studied aortic stenosis by steady state flow versus pressure drop relationships, and Starr, Schnabel, and Mayock[6] have simulated systole in cadavers Davila, Trout, Sunner, and Glover[7] have described a device that has the advantages of duplicating systole in a completely mechanical laboratory simulator The instrument described below is much simpler, smaller, and less expensive to construct than that used by Davila and his co workers, although cardiac rate and stroke output cannot be changed as easily

II DESCRIPTION OF APPARATUS

A *Ventricle and Valves*—A positive displacement pump operated at 66 strokes per minute was used as the analogue of the left ventricle (Figs 1 and 2) The chamber consisted of a thin walled gum rubber tube (2 4 cm diameter by 1 5 mm wall by 19 cm active length) compressed between the base plate and pressure plate, the latter being actuated through a follower by a motor driven cam Cardiac rate could be changed by adjusting the motor gear ratio The shape of the cam was designed so that, as it traveled through 80 degrees of rotation (22 per cent of the cardiac cycle), liquid was forced from the ventricle according to Curve 1 in Fig 3, *A* In order to study valves intended for dog implantation, Curve 1 (Fig 3, *A*) is Wiggers' ejection curve scaled down to a 30 ml stroke output (Other stroke volumes can be obtained with different cams) The slope of ejection curve at any instant is the ejection flow rate at that instant Curve 1′ of Fig 3, *B* is the derivative or "slope plot" of Curve 1 and as such it is the flow rate versus time relationship Curves 2 and 2′ in Fig 3 show the actual values obtained with the simulator

The inflow end of the ventricle was fitted with a ball check valve as a mitral substitute The outflow end of the ventricle was connected to the aortic valve holder To establish reference curves, a ball check aortic valve was used, this being replaced by a Lucite chamber containing an experimental prosthetic valve for evaluation

B *Aorta*—In normal young adult man and in the dog, an approximately straight line relationship exists between aortic pressure and aortic volume

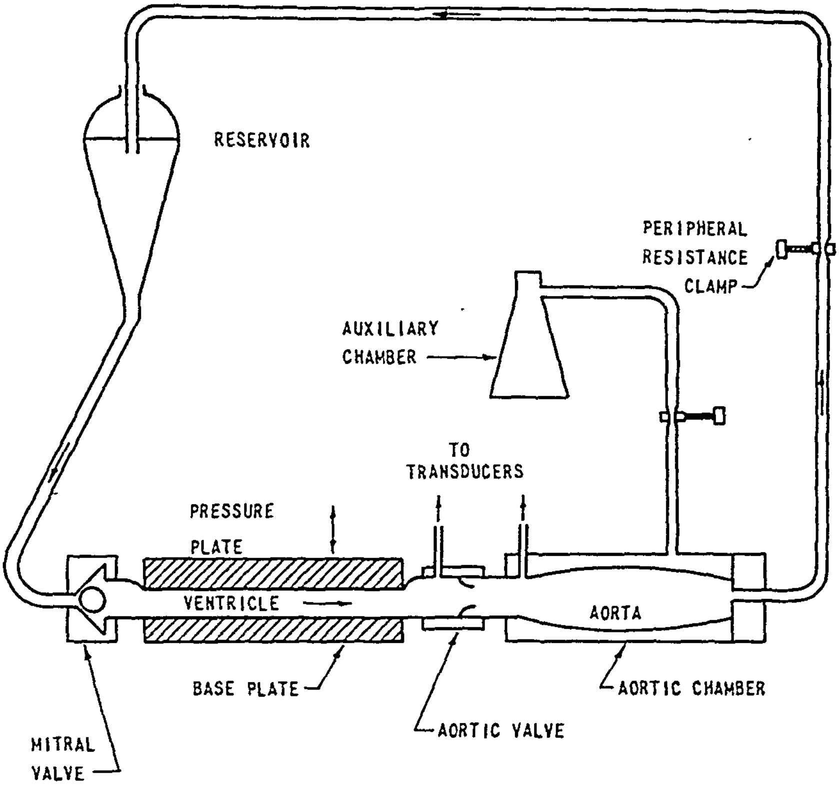


Fig. 1.—Cardiovascular simulator.

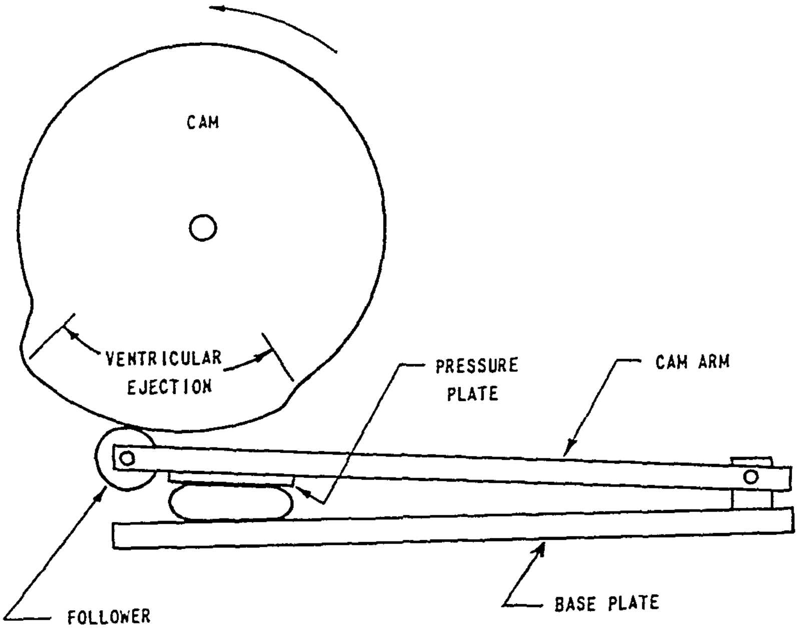
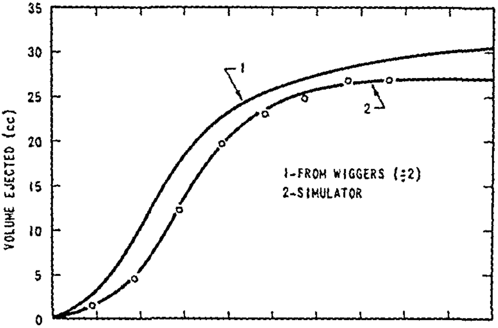
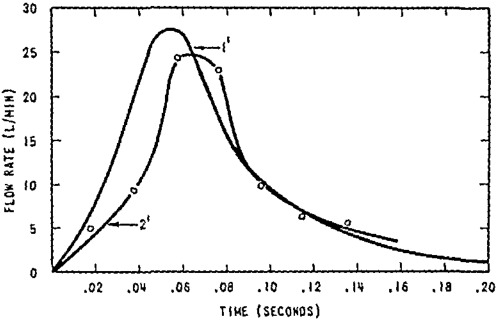


Fig. 2.—Ventricle analogue.

within the physiologic range. It can be shown by the principles of stress analysis that a straight-line relationship does not exist between volume and pressure for a thin-walled cylinder of perfectly elastic* material. The actual aortic pressure-volume curve, therefore, although simple in appearance, is a manifestation of the complex nature of the vessel walls.



A. VENTRICULAR EJECTION



B. BLOOD FLOW RATE

Fig 3—Ejection phase.

Another factor which greatly complicates the accurate simulation of blood flow is the relatively slow propagation of the arterial pulse along the aorta. If the aorta were acting as a simple container, there would be an equal increase in diameter along the entire vessel, and no traveling pulse would exist. It is known, however, that the root of the aorta distends to accommodate a relatively large volume of blood during ventricular ejection, and that the area of distention travels down the aorta at a rate of 4 to 5 meters per second. Since this involves complex transient phenomena, empirical techniques were employed to obtain normal aortic behavior.

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*As used here, elasticity is an explicit term which refers to the direct proportion of stress (tension force) to strain (deformation of a material under stress).

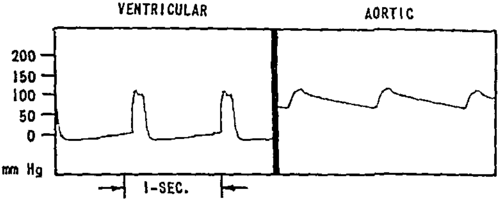
The aortic analogue consisted of gum rubber tubing (2.4 cm. diameter by 1.5 mm. wall) enclosed in an air chamber (7 cm. diameter by 26 cm. long). The volume of the air chamber was varied by partially filling it with water, and fittings were provided to allow adjustment of the gas pressure. A 500 ml. auxiliary air bottle was connected to the aortic chamber through a rubber tube to which a screw clamp was applied to restrict the passage of air. Experimentation showed that a simple air chamber could not be used for obtaining normal aortic pressure curves. When the size of the chamber was made large enough to result in proper aortic pulse pressures, the separation between the systolic and diastolic phases was lost, and the curve acquired a "saw-tooth" shape. Reducing the air volume so as to obtain a normally shaped curve resulted in high pulse pressures. It was empirically found that by reducing the aortic chamber air volume, connecting this chamber to an auxiliary chamber through an air restriction, and reducing the pressure of the air system, that nearly normal aortic curves could be produced.

C. *Peripheral Resistance and Blood Viscosity.*—Peripheral resistance was applied to the system by a screw clamp on the rubber tube leading from the aorta to the liquid reservoir. The reservoir was placed approximately 40 cm. above the ventricle so as to provide sufficient diastolic fill pressure.

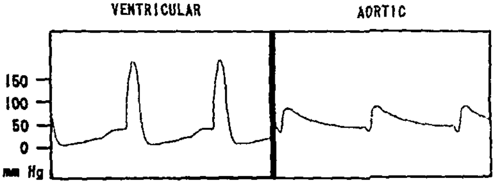
Viscosity is usually regarded as a property of a particular liquid, which changes only with composition and temperature. The viscosity of blood, however, depends also on flow conditions. Lamport[5] concluded that blood acts as a combined viscous-plastic fluid, and the in vitro performance of whole blood is such that its effective viscosity is a function of flow velocity and vessel diameter, the effect of these parameters on viscosity being more pronounced at higher hematocrit. Blood of less than 55 per cent hematocrit which flows in tubes, 3 mm. or greater in diameter, exhibits nearly pure viscous properties. From the standpoint of ventricular and aortic dynamics, therefore, the laws of viscous fluids apply. A 42 per cent glycerol solution was used as the blood analogue. At 20° C. such a solution has a viscosity of 4.1 centipoise, and at 25° C. the viscosity is 3.5.

D. *Instrumentation.*—Large bore tubes were used to communicate ventricular and aortic pressures to Statham P23A strain gauge transducers. The ventricular recording system, which received the highest frequency components, was adjusted for slight underdamping to assure maximum frequency pass band without introducing significant artifact. Step input pressure tests indicated that at this condition the response was 3 db down at 12 c.p.s., and the resonant frequency was 45 c.p.s. The recording system, which was thus capable of reproducing more than the tenth harmonic of the fundamental, was adequate for physiologic pulses.[3, 8]

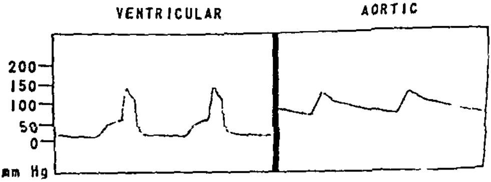
The output of each transducer circuit was fed to a cathode follower power amplifier from which three types of presentation were available: oscilloscope, recorder, and oscilloscope switch. The last facilitated a twin beam effect so that the ventricular and aortic pressures could be simultaneously displayed on the same scale. The oscilloscope (Hewlett-Packard Model 130A) was used for calibration and for adjusting the simulator variables. Permanent charts were made with a two channel Brush Electronic Oscillograph (Model BL-202 recorder with Model BL-932 DC amplifier).



A. BALL CHECK VALVE



B. TEST VALVE (LEAFLET)



C. HUFNAGEL VALVE

Fig. 4.—Pressure curves

III. METHOD OF VALVE EVALUATION

In order to establish reference curves and set the mechanical adjustments, the cardiovascular simulator was first operated with a ball check aortic valve. After the glycerol circuit was purged of air, 530 ml. of water were placed in the aortic air chamber. Previous tests indicated that this reduction in chamber volume was necessary to achieve normal aortic distensibility. The air pressure in the chamber was then reduced to 130 mm. Hg below atmospheric pressure, a value which was also determined empirically. The simulator motor was started, and the peripheral resistance clamp adjusted until the desired diastolic pressure was obtained as indicated by the aortic pressure wave displayed on the oscilloscope. The clamp on the tube between the aortic chamber and the auxiliary bottle was then adjusted for the desired systolic pressure.

The above procedure established a "normal" cardiovascular system, and recorder charts were taken of the ventricular and aortic pressure curves (Fig. 4, *A*). The ball check valve was then removed and a test prosthetic aortic valve put in its place, care being taken that none of the simulator adjustments were moved. Pressure waves were recorded with the test valve in the otherwise "normal" cardiovascular system. Fig. 4, *B* shows the tracings from a cast leaflet type synthetic elastomer valve,* a high degree of stenosis being obvious. A Hufnagel valve[4] showed only slight stenosis (Fig. 4, *C*). As a confirmation of test reliability, the ball valve was reassembled in the simulator and pressures recorded. These charts were compared to the initial tracings to determine whether the simulator adjustments remained unchanged during the test.

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*Designed by William Hall, M.D., resident in surgery, University of Kansas Medical Center, Kansas City, Kan.

Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Fortieth Annual Meeting of The American Association for Thoracic Surgery will be held May 11, 12, and 13, 1960, in Miami Beach, Florida Headquarters will be the Deauville Hotel

Requests for Hotel Reservations

These should be mailed directly to Mrs Mildred Sander, Reservation Manager, Deauville Hotel Miami Beach, Florida Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure If accommodations are desired elsewhere please communicate directly with the hotel of your choice

Material for the Program

SCIENTIFIC PAPERS — Abstracts of all papers proposed for presentation at the 1960 meeting *must be received on or before* **November 15, 1959,** otherwise they will not be considered by the Program Committee These should be labeled "For Thoracic Surgery Forum" or "For Regular Program" depending upon the nature of the subject matter, *in the same manner* as in previous years They should contain from 200 to 250 words that accurately reflect the content of the completed paper

Six, typewritten clearly legible copies of *each* abstract must be sent to Miss Ada [illegible] Administrative Assistant, The American Association for Thoracic Surgery [illegible] Carondelet Building, 7730 Carondelet Avenue, St Louis 5, Missouri

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary *immediately* after their presentation If they are not ready at that time there is a chance that they will not be published in THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than* **November 15, 1959,** otherwise the application will be deferred for consideration until the 1961 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Frank Gerbode, M.D.
Chairman of the Membership Committee
Stanford University Hospital
San Francisco 15, California

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applicants be held over for reconsideration a *second year.*

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Original Communications

THE SURGICAL MANAGEMENT OF COMPLICATIONS OF STAPHYLOCOCCAL PNEUMONIA IN INFANCY AND CHILDHOOD

David C. Sabiston, Jr., M.D., Edward H. Hopkins, M.D. (by invitation), Robert E. Cooke, M.D. (by invitation), and Ivan L. Bennett, Jr., M.D. (by invitation), Baltimore, Md.*

STAPHYLOCOCCAL infections have assumed particular importance in recent years primarily as a result of the resistance of certain strains of the organism to antibiotics.[1-8] One of the striking features of this problem has been the increase in the incidence of staphylococcal pneumonia in infancy and childhood.[9-16] Formerly, staphylococcal pneumonia in the early years of life was an infrequent disease characterized by high mortality. A marked change has occurred in both the incidence and prognosis in the past several years. The purpose of the present communication is to report a study of staphylococcic pneumonia in pediatric patients at the Johns Hopkins Hospital over a period of 4 years. *Particular emphasis is placed on the surgical management of complications* which occurred with progression of the disease.

DESCRIPTION OF PATIENTS

General.—The material on which this study is based consists of all patients under the age of 12 upon whom a diagnosis of staphylococcic pneumonia was made during the period January, 1955, through December, 1958. During this

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Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

*Investigator, Howard Hughes Medical Institute.

time, 67 cases were observed. The age of the patients ranged from 10 days to 12 years (Table I). It is apparent that the disease was most common in the first year of life (75 per cent) with a high proportion of the cases occurring within the first 3 months.

TABLE I. AGE INCIDENCE OF STAPHYLOCOCCAL PNEUMONIA

AGE	PRIMARY	SECONDARY
0- 3 mo.	25	3
4-12 mo.	21	1
1- 6 yr.	14	2
6-12 yr.	0	1
Totals	60	7

Predisposing Factors.—In the group of 67 patients in the present study, there were 60 who had staphylococcic pneumonia as the only major illness and the pneumonia was considered to be a *primary* diseases. In 7 patients, the pneumonia accompanied another severe systemic illness and the pneumonia was considered to be a *secondary* disease. The underlying diseases in this latter group were cystic fibrosis of the pancreas, pyelonephritis, agammaglobulinemia, congenital pyloric stenosis, adrenal insufficiency, and congenital biliary atresia. Sixteen of the patients had other foci of staphylococcic infections which included pyoderma, renal abscess, osteomyelitis, and brain abscess. Only 2 in the entire group had a history of prematurity.

Manifestations.—The history in the majority of patients consisted of the sudden onset of a respiratory infection with rapid progression of symptoms. This was particularly characteristic of the younger children, many of whom were gravely ill when first seen at the hospital. In a significant number of patients, symptoms appeared following a previous simple upper respiratory infection. The manifestations noted in the entire group in order of frequency were tachypnea (61), fever (48), dyspnea (48), cough (33), abdominal distention (13), and cyanosis (12). On physical examination, dullness on the affected side of the chest and diminished breath sounds were found in approximately three fourths of the group and râles were present in approximately half the patients. Fever was present in the majority of cases and ranged between 37.5° and 40.3° C. In 11 patients, however, the initial temperature was less than 37° C.

Bacteriology.—From the majority of the patients, bacteriologic cultures were obtained from several sources including the nasopharynx, throat, blood, and material obtained on pleural aspiration. In 65 of the 67 patients, a staphylococcus *(Micrococcus pyogenes)* was obtained from one or more sources. The organism was found in 36 of 38 patients in whom pleural aspiration was performed. In those patients without empyema, a diagnosis was made on the basis of a combination of positive cultures from other sources in association with a pneumonia characterized by the formation of pneumatoceles. The culture data are presented in Table II. Antibiotic sensitivities by the disc method showed that the organisms were sensitive to novobiocin (95 per cent), chloramphenicol (92 per cent), and erythromycin (85 per cent). Few strains were susceptible to penicillin (17 per cent) or streptomycin (15 per cent).

TABLE II STAPHYLOCOCCIC PNEUMONIA

	BACTERIOLOGY		
	CASES CULTURED	CASES POSITIVE	PER CENT POSITIVE
Nasopharynx	49	44	90
Throat	43	34	79
Pleural fluid	38	36	95
Blood	38	7	19

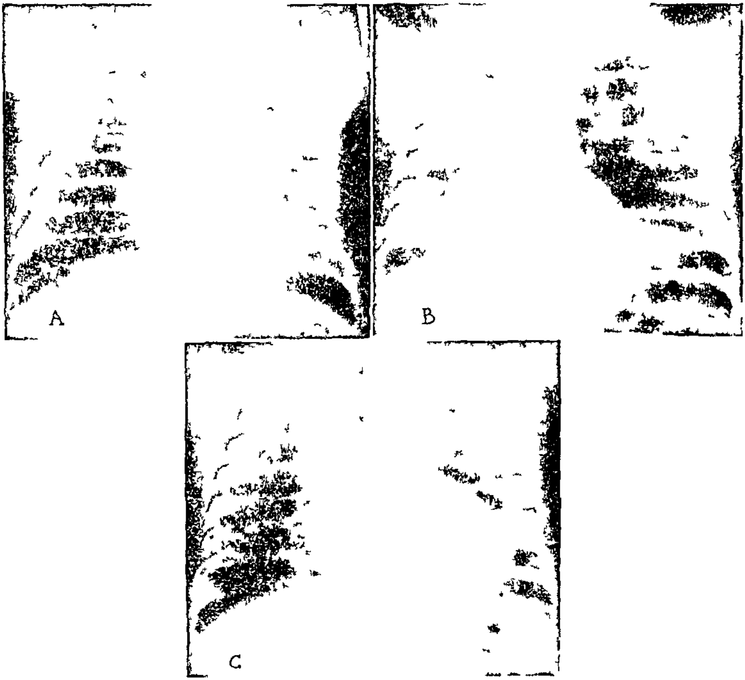

Fig 1—A Chest film which shows early staphylococcal pneumonia with development of multiple pneumatoceles in the left lung

B A tension pneumothorax developed following rupture of a pneumatocele into the pleural cavity Several large pneumatoceles remain The mediastinum and trachea are shifted to the right

C Chest film made after introduction of an intercostal catheter and re expansion of lung with relief of respiratory insufficiency

In 13 of the more recent patients, the staphylococci have been studied for their bacteriophage type The results showed that eight of the thirteen were type 52/42B/81, two were 44A, and three were untypable

Radiography—A pulmonary infiltrate was present in all cases Disease was unilateral in 58 of the 67 patients (87 per cent) Pleural fluid was observed in 48 patients (72 per cent) An example of this is shown in Fig 3, A

Empyema characteristically began as a thin layer of fluid present at the periphery of the film. Another feature of the radiologic picture was the early development of small pneumatoceles in or near the area of pneumonic infiltration. An example of this is shown in Fig. 1, *A*. Pneumatoceles were observed in 56 of the 67 patients (84 per cent). With the progression of the disease, the pneumatoceles frequently increased in size and, in 15 patients (23 per cent), ruptured into the pleural cavity. The resulting pneumothorax with shift in the mediastinum produced respiratory distress (Fig. 1, *B*). In a small number of patients, a pneumatocele became filled with purulent material and behaved as a

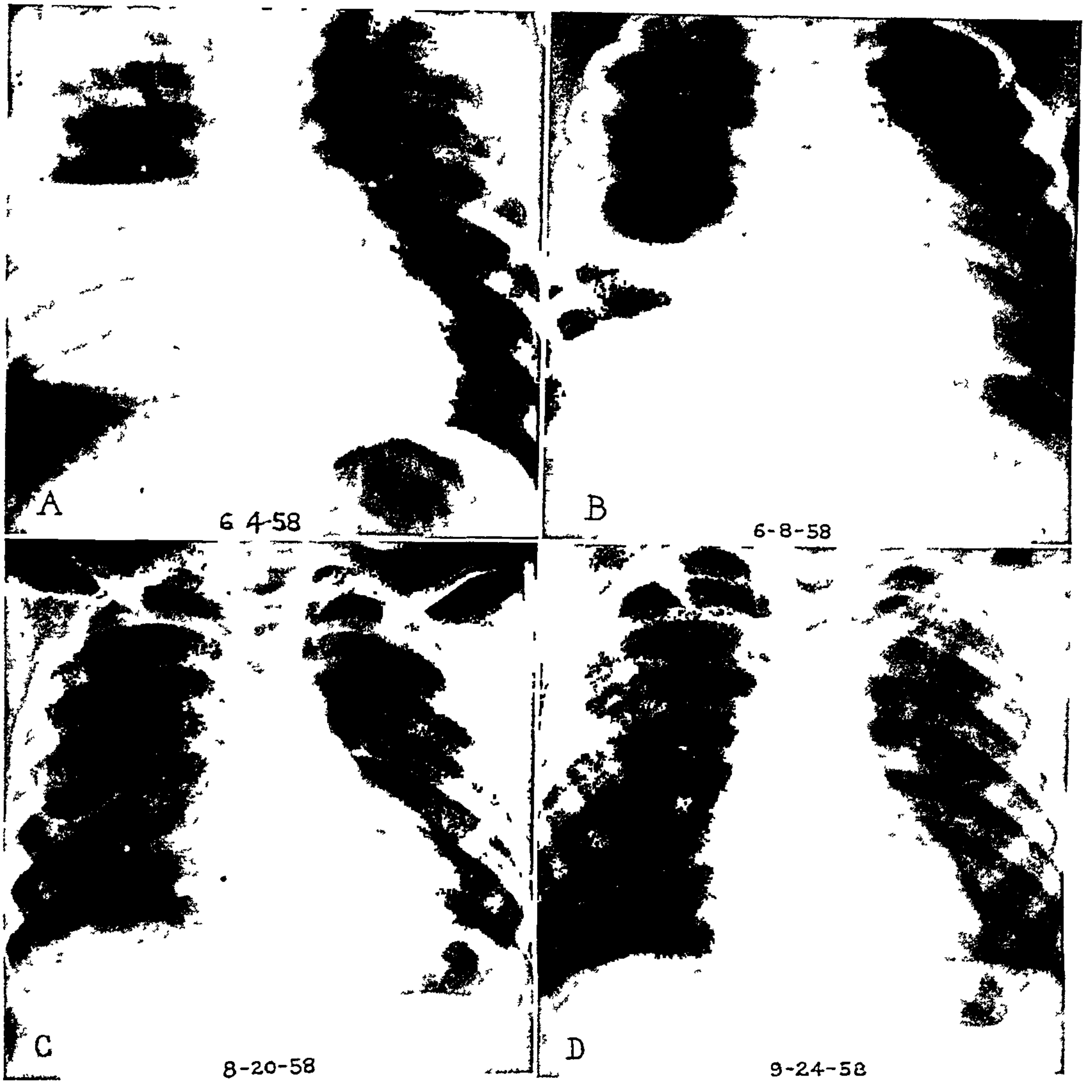

Fig 2.—*A*, Chest film which demonstrates massive pneumatocele with fluid level The patient showed marked evidence of infection and drainage appeared mandatory. The pneumatocele extended to the parietal pleura

B, The cavity was drained by the introduction of an intercostal catheter with marked symptomatic relief.

C, Chest film made 11 weeks later showing persistence of pneumatocele The patient was asymptomatic

D, Complete disappearance of pneumatocele 15 weeks after onset of staphylococcal pneumonia.

lung abscess An example of this complication is shown in Fig 2, A In this instance the cavity had a peripheral border near the parietal pleura and it was possible to drain the purulent material through a catheter introduced by the use of an intercostal trocar (Fig 2, B)

Refractory empyema with collapse of the lung and development of fibrotic pleurisy was rare, being observed in only 1 patient In this case, thoracotomy with pulmonary decortication was followed by complete recovery (Fig 3) A survey of the radiologic findings in the entire group is presented in Table III

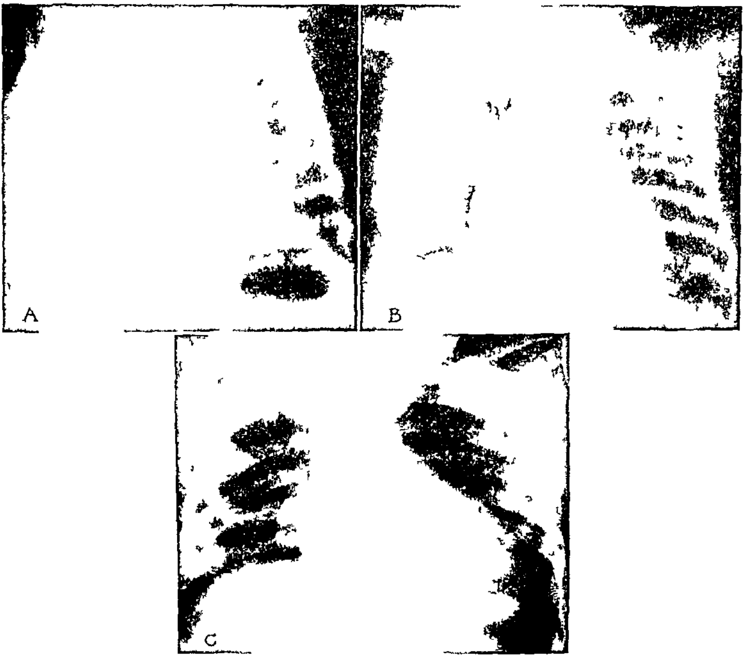

Fig 3 — A, Chest film which shows acute staphylococcal pneumonia of right lung with empyema An intercostal catheter was employed for drainage of the empyema

B, Injection with contrast medium 4 months later following failure of lung to expand A large empyema cavity is shown A large portion of the right lung is collapsed.

C, Chest film made after right thoracotomy and pulmonary decortication The right lung has completely re expanded.

TABLE III RADIOLOGIC FINDINGS IN 67 CASES OF STAPHYLOCOCCAL PNEUMONIA

	NUMBER	PER CENT
Empyema	48	72
Pneumatoceles	56	84
Pneumothorax	15	23
Unilateral disease	58	87
Bilateral disease	9	13

Antimicrobial Drugs.—The treatment of staphylococcal pneumonia is primarily medical and antibiotics should be administered in large amounts. The usual initial therapy in the present study consisted of chloramphenicol and novobiocin. The majority of the patients also received penicillin as the bactericidal antibiotic of choice. Despite the low percentage of susceptible organisms as shown by the disc sensitivity method, large doses of this drug are often effective.[17] In the group of 67 patients studied, chloramphenicol was administered in 56 (84 per cent), penicillin in 49 (73 per cent), erythromycin in 28 (42 per cent), novobiocin in 28 (42 per cent), and streptomycin in 4 (6 per cent). The actual amount varied considerably for each of the drugs depending on the weight of the child and the severity of the illness. The usual daily dosage was penicillin 2 to 10 million units, chloramphenicol 100 mg./Kg., erythromycin 50 mg./Kg., and novobiocin 50 mg./Kg.

Supportive Therapy.—The use of a high humidity-high oxygen atmosphere and judicious infusion of intravenous fluids with correction of electrolyte imbalance are helpful in the management of staphylococcic pneumonia. The administration of gamma globulin in large doses (0.2 Gm. per kilogram of body weight) to infants under 1 year of age may be indicated because of the presence of physiologic hypogammaglobulinemia.

Surgical Aspects.—Needle aspiration of the chest was performed in 48 (73 per cent) of the 67 patients. This procedure frequently leads to an immediate bacteriologic diagnosis. In addition, the removal of purulent material from the pleural cavity was of definite therapeutic benefit in many instances and may prevent the development of more serious complications. In 28 patients (43 per cent), an intercostal catheter was inserted under local anesthesia either for drainage a large empyema the relief of a tension pneumothorax or a combinat th (Table I example of the use of closed catheter

TABLE IV. CAL PNEUMONIA

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otherwise normal. A film showed an accumulation of fluid and air in the right chest with a shift of the mediastinum to the left (Fig 3, *A*). A thoracentesis was performed with removal of the air and purulent material. A smear of the pleural aspirate showed gram positive cocci which later proved on culture to be hemolytic *Staphylococcus aureus*. An intercostal catheter was introduced under local anesthesia with further removal of air and obvious improvement in respiratory function. Penicillin and erythromycin were begun and the child's condition rapidly improved. Within several days it became necessary to introduce additional catheters in an effort to drain more adequately the empyema. This was not successful and it was eventually necessary to institute open drainage by rib resection. An excellent clinical response followed and the patient was discharged from the hospital. On June 14, 1956, she was re-admitted due to persistent drainage from the empyema cavity. Instillation of radiopaque medium showed a large chronic empyema cavity (Fig 3, *B*). A right thoracotomy was performed and a thick, fibrotic pleura was found covering the entire lung. A pulmonary decortication was performed with complete expansion of each of the three lobes. Following operation the child did well and became completely asymptomatic. A final chest film is shown in Fig 3, *C* and is essentially normal.

RESULTS

The cases studied in the present series were divided into *primary* and *secondary* groups. There were 60 patients in the primary group and of these 5 died (8 per cent) (Table V). Of the 7 patients in the secondary group, all succumbed.

An analysis of the 5 deaths in the *primary* group reveals that in each instance the child was in the younger group, being 1 year or less of age, and 4 of the 5 were under the age of 3 months (Table V). Four of the 5 infants died within 72 hours after admission. Three had bilateral pneumonia (Table VI).

TABLE V MORTALITY IN PRIMARY STAPHYLOCOCCAL PNEUMONIA BY AGE GROUPS

AGE RANGE	CASES	PER CENT MORTALITY
0-3 mo	25	17
4-12 mo	21	5
1-6 yr	14	0
Over 6	0	0
Totals	60	8

TABLE VI MORTALITY IN PRIMARY STAPHYLOCOCCAL PNEUMONIA

CASE	AGE	EXTENT OF PNEUMONIA	PLEURAL CULTURE	INTERCOSTAL CATHETER	DAY OF DEATH*	AUTOPSY
D J	13 da	Empyema with pneumatoceles, left	+	+	1	Pneumonia abscess, and empyema of left lung
A P	1 yr	Bilateral empyema and left pneumothorax	+	+	2	None
S C	2 mo	Bilateral pneumonia and right empyema	+	0	1	None
E K	5 wk	Bilateral empyema	+ (autopsy)	0	3	Multiple, bilateral pulmonary abscesses and bilateral empyema
R A	2½ mo	Right empyema and pneumatoceles	+	+	18	Pneumonia, empyema, and abscess, right lung

*Days after admission

Antimicrobial Drugs.—The treatment of staphylococcal pneumonia is primarily medical and antibiotics should be administered in large amounts. The usual initial therapy in the present study consisted of chloramphenicol and novobiocin. The majority of the patients also received penicillin as the bactericidal antibiotic of choice. Despite the low percentage of susceptible organisms as shown by the disc sensitivity method, large doses of this drug are often effective.[17] In the group of 67 patients studied, chloramphenicol was administered in 56 (84 per cent), penicillin in 49 (73 per cent), erythromycin in 28 (42 per cent), novobiocin in 28 (42 per cent), and streptomycin in 4 (6 per cent). The actual amount varied considerably for each of the drugs depending on the weight of the child and the severity of the illness. The usual daily dosage was penicillin 2 to 10 million units, chloramphenicol 100 mg./Kg., erythromycin 50 mg./Kg., and novobiocin 50 mg./Kg.

Supportive Therapy.—The use of a high humidity-high oxygen atmosphere and judicious infusion of intravenous fluids with correction of electrolyte imbalance are helpful in the management of staphylococcic pneumonia. The administration of gamma globulin in large doses (0.2 Gm. per kilogram of body weight) to infants under 1 year of age may be indicated because of the presence of physiologic hypogammaglobulinemia.

Surgical Aspects.—Needle aspiration of the chest was performed in 48 (73 per cent) of the 67 patients. This procedure frequently leads to an immediate bacteriologic diagnosis. In addition, the removal of purulent material from the pleural cavity was of definite therapeutic benefit in many instances and may prevent the development of more serious complications. In 28 patients (43 per cent), an intercostal catheter was inserted under local anesthesia either for drainage of a large empyema or for the relief of a tension pneumothorax or a combination of both (Table IV). An example of the use of closed catheter drainage in a patient with a large empyema collection in a massive pneumatocele is shown in Fig. 2. Similar drainage for a tension pneumothorax following the rupture of a subpleural pneumatocele is shown in Fig. 1. The use of an intercostal catheter was sufficient to drain the empyema in all instances except one. Open drainage by rib resection and pulmonary decortication for fibrothorax with compression of the right lung was necessary, as illustrated in the following case.

TABLE IV. STAPHYLOCOCCAL PNEUMONIA

Thoracentesis	48 (73%)
Intercostal catheter	28 (43%)
Open chest drainage	1
Pulmonary decortication	1

Case history: A 1-month-old white female was admitted to the Johns Hopkins Hospital on Feb. 1, 1956, with a history of sudden onset of severe pharyngitis the previous day. She had been treated by her pediatrician with an injection of penicillin. On the day of admission the infant was found quite dyspneic and cyanotic in bed. On examination, the temperature was 37.8° C. and marked dyspnea and cyanosis were present. The right chest was dull to percussion and no breath sounds were heard. The left chest was hyperresonant but otherwise normal. A film showed an accumulation of fluid and air in the right chest with a shift of the mediastinum to the left (Fig 3, A). A thoracentesis was performed with removal of the air and purulent material. A smear of the pleural aspirate showed gram-positive cocci which later proved on culture to be hemolytic *Staphylococcus aureus*. An intercostal catheter was introduced under local anesthesia with further removal of air and obvious improvement in respiratory function. Penicillin and erythromycin were begun and the child's condition rapidly improved. Within several days it became necessary to introduce additional catheters in an effort to drain more adequately the empyema. This was not successful and it was eventually necessary to institute open drainage by rib resection. An excellent clinical response followed and the patient was discharged from the hospital. On June 14, 1956, she was re-admitted due to persistent drainage from the empyema cavity. Instillation of radiopaque medium showed a large chronic empyema cavity (Fig. 3, B). A right thoracotomy was performed and a thick, fibrotic pleura was found covering the entire lung. A pulmonary decortication was performed with complete expansion of each of the three lobes. Following operation the child did well and became completely asymptomatic. A final chest film is shown in Fig. 3, C and is essentially normal.

RESULTS

The cases studied in the present series were divided into *primary* and *secondary* groups. There were 60 patients in the primary group and of these 5 died (8 per cent) (Table V). Of the 7 patients in the secondary group, all succumbed.

An analysis of the 5 deaths in the *primary* group reveals that in each instance the child was in the younger group, being 1 year or less of age, and 4 of the 5 were under the age of 3 months (Table V). Four of the 5 infants died within 72 hours after admission. Three had bilateral pneumonia (Table VI).

TABLE V. MORTALITY IN PRIMARY STAPHYLOCOCCAL PNEUMONIA BY AGE GROUPS

AGE RANGE	CASES	PER CENT MORTALITY
0-3 mo	25	17
4-12 mo	21	5
1-6 yr	14	0
Over 6	0	0
Totals	60	8

TABLE VI. MORTALITY IN PRIMARY STAPHYLOCOCCAL PNEUMONIA

CASE	AGE	EXTENT OF PNEUMONIA	PLEURAL CULTURE	INTERCOSTAL CATHETER	DAY OF DEATH*	AUTOPSY
D. J.	13 da	Empyema with pneumatoceles, left	+	+	1	Pneumonia, abscess and empyema of left lung
A. P.	1 yr	Bilateral empyema and left pneumothorax	+	+	2	None
S. C.	2 mo.	Bilateral pneumonia and right empyema	+	0	1	None
E. K.	5 wk	Bilateral empyema	+ (autopsy)	0	3	[illegible]
R. A.	2½ mo	Right empyema and pneumatoceles	+	-	1	[illegible]

---

*Days after admission

In the *secondary* group, the primary diseases included cystic fibrosis of the pancreas, nephritis, agammaglobulinemia, adrenal insufficiency, congenital hypertrophic pyloric stenosis, and biliary atresia. In 2 patients, the pneumonic process involved both lungs and in 5 others it was unilateral (Table VII).

TABLE VII. MORTALITY IN SECONDARY STAPHYLOCOCCAL PNEUMONIA

CASE	AGE	PRIMARY DISEASE	EXTENT OF PNEUMONIA	PLEURAL CULTURE	INTERCOSTAL CATHETER	AUTOPSY
L. J.	1 mo.	Cystic fibrosis of pancreas	Left pneumonia, pneumatoceles, and empyema	+	0	Cystic fibrosis of pancreas; multiple abscesses of left upper lobe and left empyema
D. H.	4 mo.	Hypoprothrombinemia; pyelonephritis (GU anomaly)	Bilateral pneumonia	Not done	0	Pneumothorax and multiple lung abscesses; congenital anomaly of renal pelvis
C. C.	5 yr.	Agammaglobulinemia, bilateral mastoiditis, and brain abscess	Right pneumonia, empyema and pneumatoceles	+	+	Multiple brain abscesses and hemorrhage in parietal lobe; right empyema and bilateral pneumonia
R. F.	2 mo.	Congenital hypertrophic pyloric stenosis	Right pneumonia and pneumothorax	+	+	Congenital hypertrophic pyloric stenosis; bilateral pneumonia and empyema; multiple lung abscesses
D. L.	3 mo.	Cystic fibrosis of pancreas	Right empyema and pneumonia	+	0	Cystic fibrosis of pancreas; right empyema and pneumonia
C. G.	1 mo.	Adrenal insufficiency	Right pneumonia and abscess	+	0	Bilateral, massive adrenal hemorrhage (history of adrenal insufficiency since birth); right pneumonia and abscess
C. N.	21 mo.	Congenital biliary atresia	Bilateral pneumonia	Not done	0	None (congenital biliary atresia at exploratory laparotomy and confirmed by liver biopsy)

DISCUSSION

The problem of staphylococcic infection has assumed renewed importance in recent years. The details of the development of resistance to antibiotics by this group of organisms and their role in nosocomial infection are so familiar as to require no repetition here. Several excellent reviews are available.[5-8]

Pneumonia in childhood due to the staphylococcus has been long regarded as a serious disease which is frequently attended by a number of serious complications. In the pre-antibiotic era, the mortality, particularly during infancy, was quite high. In 1936, MacGregor[18] reported 10 proved cases in which all the patients died. The sulfonamides initially offered some protection but with the introduction of penicillin significant improvement in the results occurred. Kanof and associates,[19] in 1953, reported a group of children with staphylococcic pneumonia treated with sulfonamides alone and found the mortality to be 50 per cent; when sulfonamide was combined with penicillin the mortality fell to 25 per cent. More recent studies have reported a mortality between 0 and 31 per cent.[9, 11, 21]

The primary therapy in staphylococcic pneumonia consists of the administration of antibiotics. In the past, penicillin was the agent of choice but, with the increasing incidence of "penicillin resistant organisms," the other antibiotics, including chloramphenicol and erythromycin, have been frequently employed either singly or in combination. In the present series the organisms were chiefly sensitive to chloramphenicol, erythromycin, and novobiocin and these antibiotics were used in most instances. In addition penicillin was administered to many of the patients in recognition of the fact that the staphylococcus may often be sensitive to high concentrations of this *bactericidal* agent. In many instances, the disc method shows resistance to penicillin whereas higher concentrations in serial dilutions will demonstrate sensitivity.[17] Penicillin in high dosage was administered in association with other antibiotics in 73 per cent of the patients in this series.

The role of surgery in staphylococcic pneumonia is confined to the [illegible] ment of complications which occur with the progression of th [illegible] basic pathologic process in this type of pneumonia is [illegible] necrosis with abscess formation which can involve a lobe or an entire lung. Pleural empyema tends to appear early. The abscesses often enlarge and obstruct or involve directly the bronchioles and smaller bronchi. Tension blebs (pneumatoceles) are thus created in a high percentage of cases. Pneumatoceles are particularly likely to form in children and those just beneath the pleura often perforate and produce a tension pneumothorax. Pyopneumothorax is almost diagnostic of staphylococcic infection in pediatric patients.

Aspiration of the purulent material from the pleural cavity is of diagnostic aid, relieves the toxic manifestations of undrained staphylococcic pus, and permits expansion of the lungs. The necessity for drainage of the pleural cavity is determined by the thickness and amount of purulent material as well as the toxicity of the patient. Continuous pleural drainage is not indicated, however, in all cases of empyema. In the present study, empyema was present in 48 patients (72 per cent), and intercostal drainage was performed in 28 (43 per cent) and, of these, 15 (23 per cent) had associated pneumothorax. Early and adequate drainage of pus will prevent the development of the more troublesome fibrothorax and the necessity for pulmonary decortication. In virtually all cases, adequate drainage can be accomplished by the introduction of an intercostal catheter through a trocar. The consistent effectiveness of closed drainage in staphylococcal empyema in infants differs considerably from the s [illegible] n countered in adults, in wh [illegible] drainage with rib resection is necessary. Closed intercostal drainage may be lifesaving when performed as an emergency procedure for the relief of tension pneumothorax. This complication occurred in 23 per cent of the patients studied in the present series and occurred on repeated occasions in several patients. Tension may also occur in a pneumatocele and require catheter drainage, as emphasized by Watkins and Hering.[22] The introduction of a catheter into the chest through a trocar is simple and easily performed. Complications from the procedure are rare when it is performed carefully. This method may be highly recommended in the management of the complications of staphylococcal pneumonia and has been endorsed in recent publications as the procedure of choice by Bloomer and associates,[10] Hertzler, Miller, and Tuttle,[20] and Watkins.[13]

Another complication which may occur in patients in whom an empyema becomes chronic is fibrotic pleurisy (fibrothorax) producing partial pulmonary collapse ("captive lung"). When this occurs, open thoracotomy with complete pulmonary decortication should be employed without hesitation. This procedure will rarely be necessary if the empyema is adequately drained and the lung re-expanded early in the course of the disease by proper selection of initial therapy.

The results obtained in staphylococcal pneumonia in infancy and childhood in this and other recent series are encouraging. An analysis of the 12 deaths which occurred in the 67 cases reported here indicates that fulminating infections or other complicating disease, rather than recognizable surgical complications, were important in the outcome. Much progress has been made in the early recognition and surgical management of the pulmonary tension and suppurative complications of a staphylococcal pneumonia, and death as a result of such problems should be rare. The hope at present is for further advance in the medical management of those patients with rapidly progressive disease characterized by severe toxic manifestations in the first few months of life.

SUMMARY

A definite increase in the incidence of staphylococcal pneumonia in the pediatric age group has occurred during the past several years. A group of 67 patients was studied, and the incidence and management of surgical complications have been evaluated. Continuous drainage by the closed technique was employed in the more severe cases of empyema with good results. The development of tension pneumothorax demands immediate catheter drainage for decompression and re-expansion of the lung. Proper selection of therapy early in the course of the disease prevents the development of more severe complications such as chronic empyema and fibrothorax. The prognosis in primary staphylococcal pneumonia is good and the mortality is largely confined to the group, under the age of 3 months, with overwhelming infection. In those instances in which the disease is secondary to another severe systemic illness, the prognosis is quite poor.

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DISCUSSION

DR RICHARD H MEADE, Grand Rapids, Mich—I think that was a very excellent presentation of a very important subject The only reason I arise is to supplement what has been said

I heard the speaker refer to an article in 1936 He did not refer to the article written by Neuhof in 1930, I believe it was, in which he discussed this subject especially among infants and young children I didn't look up the figures before I came here, so I may be wrong, but my impression is that in that early day, before sulfonamides and antibiotics his mortality rate was about the same as that reported today

I think it is important for those men in the audience who have grown up in the antibiotic era to realize that one could do surgery in the days before the antibiotics, and that the treatment of empyema is today essentially the same as it was then It is establishing adequate drainage at the proper time

I think this is a very interesting paper, as I said before

DR. JOHN M. SNYDER, Bethlehem, Pa.—I would like to compliment Dr. Sabiston and his group on their very respectable mortality rate. My personal experience has been limited to about a third of this number of patients, all of whom had surgical complications. Unfortunately, the mortality was about triple that reported.

About 1 in 4 had bilateral disease and the results were rather uniformly fatal. Of the ones with unilateral disease who died one of them did show at postmortem an interesting complication of a mediastinal abscess. I would like to present at this time a rather interesting case of a patient in whom there was a delay of approximately a month in the appearance of a major complication.

(Slide) Incidentally, our deaths were all in patients under the age of 6 months. This slide shows a six-month-old female infant with early disease in the right side which 2 days later showed a typical pneumothorax. A catheter was placed in the chest (slide) and 2 days later the film showed satisfactory expansion of the lung (slide), and 1 week later, after removal of the catheter, the child was doing fairly well on intravenous Spontin and chloromycetin.

(Slide) There was nothing of much note except to see some early pneumatoceles forming to the right of the heart, and 1 week later, prior to discharge, they were a little bit larger, but the child was having no particular difficulty, seemed to be clinically well, and was returned home under the care of the pediatrician.

(Slide) Two weeks later the child suddenly had severe dyspnea and was brought into the hospital, and now this slide shows tension pneumatoceles with deviation of the mediastinum, pushing the heart over to the left with an anterior mediastinal herniation.

(Slide) Catheters were placed into the right chest, but unfortunately we did not seem to have them in the proper place initially. One was in a pneumatocele; one was in the pleural space.

(Slide) An additional catheter was placed into the larger pneumatocele (it doesn't show too well on this slide) but there was beginning now to be a return of the mediastinum to the normal position.

(Slide) Increasing the suction on the catheters, 1 week later we had a rather respectable looking chest.

(Slide) Two weeks later I was out of town and a friend who was looking after the patient was loathe to remove the catheter. At this point, the catheter had been clamped for a week. There was no obvious recurrence of the pneumatocele; the catheter was removed, and the child remained well and has been well since.

There was fully a month's delay before the development of the tension pneumatocele, and I think it illustrates the need for vigilance over a considerable period of time in these cases.

DR. GABRIEL P. SELEY, New York, N. Y.—As has already been mentioned, this disease was extensively described by Dr. Neuhof in the early 1930's. I had the privilege of working with him at that time and continued to work with him for many years.

I would like to mention briefly one complication that has not been stressed today, and that is a chronic staphylococcic empyema. At the termination of the treatment for the acute empyema, whether it be by catheter drainage, rib resection, or even decortication, these patients will often develop a chronic empyema. This is manifest after approximately 3 months by a residual shadow in the pleural cavity, commonly termed thickened pleura. I know if Dr. Neuhof were here he would make this much more dramatic than I am doing it, because one word he never could stand was ''thickened'' pleura. Thickened pleura to him always meant a chronic empyema if it lasted for more than 3 months after the treatment of a ''staph'' empyema.

Now, if there are some shadows in the lower chest, that is, distortion of the diaphragm or some adhesions, that was acceptable, but if there was anything which really represented a thickened pleura, this actually means a chronic pleuritis or empyema.

We have had cases now with free intervals as long as 5 years, several cases up to 10 years and, within the last 2 months, a patient entered the hospital who had a chronic empyema who had had no symptoms for 34 years At operation this turned out to be a chronic staphylococcic empyema. The treatment of chronic empyema is drainage with or without decortication as indicated

DR. THOMAS C. MOORE, Indianapolis, Ind—I wish to compliment Dr. Sabiston on a very interesting and valuable study I should like to confine my comments to one phase of the complications of staphylococcal pneumonia in infancy and childhood, that relating to the formation of post pneumonic pulmonary abscess formation

Last fall I reported an experience with four lobectomies carried out for post pneumonic lung abscess in infants and children In all of these cases the abscess was due to hemolytic *Staphylococcus aureus* This made us somewhat curious as to the occurrence of a number of cases of lung abscess due to this organism, and we reviewed, Dr Battersby and I, the experience at the Indiana University Medical Center with pulmonary abscess during a period of 25 years. This review is just nearing completion.

We found a total of 49 cases of pulmonary abscess in infancy and childhood However, the majority of these cases occurred as diffuse and often miliary abscess formations Only 18 were isolated pulmonary abscesses. Fourteen of these cases of pulmonary abscess occurred prior to 1948 and only 4 since that time

We also were interested in the number of cases which were post pneumonic Most reports suggest that post pneumonic abscess in infants and children is rather rare and when abscess formation does occur, that it usually occurs as a postoperative complication We *found that, of our 18 cases of isolated pulmonary abscess,* 12 were *post pneumonic* 2 were due to foreign bodies, 2 to aspiration, and 2 others to feeding problems and to mental deficiency.

The bacteriology in the post pneumonic abscesses was of considerable interest to us We had bacteriologic studies available in 11 of the 12 cases of post pneumonic abscess Six of these were due to *Staphylococcus aureus* One was due to *Staphylococcus albus,* and 4 to streptococcus

The majority were managed by nonoperative measures since they occurred largely in the pre antibiotic era. Eleven cases were so managed. Seven of these occurred in the pre antibiotic era and all 7 died. Four were managed medically with antibiotics and 2 of these died for a mortality of 50 per cent Surgery was carried out in 7 cases, rib resection with drainage in 1, and pulmonary resection in 6 All 7 of these patients survived. We felt that these results of operative as compared with nonoperative means were of some interest

The deaths in the non operatively managed cases were largely due to brain abscess and purulent meningitis. These complications occurred in 5 of the 9 deaths

Although few of the cases of staphylococcal pneumonia, in which pulmonary abscess occurs, may come to operative intervention of a resectional nature, we feel that resection should be carried out if the abscess does not respond to appropriate, vigorous antibiotic therapy, or if it does respond and a largely destroyed lung remains as a sterile cystic mass

DR ROBERT J JENSIK, Chicago, Ill.—I would like to ask the authors if all of their experiences with residual pneumatoceles responded as beautifully as the one that was demonstrated.

I bring up this point because in the past year we have seen 4 infants, all under a year of age, in which the air space, instead of disappearing, enlarged to the point where practically no visible lung parenchyma was seen, and with some reluctance we did place catheters in these pneumatoceles

We realized that a possible pleural space problem was apt to develop, in addition to the drainage of this pneumatocele, but in all cases we were able to see a reduction in size of the pneumatocele with eventual complete resolution at a rather fast rate.

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DR. DAVID WATKINS, Denver, Colo.—I wish to congratulate Dr. Sabiston and his associates for a most enlightening and valuable contribution to our understanding of this disease.

This disease may be primarily bronchogenic and develop by intracanalicular spread, or it may be hematogenous.

(Slide) Gradations are seen here between zones of necrotizing pneumonitis and acute microabscess formation. These microabscesses become confluent and form larger consolidated abscess cavities. Pleural surfaces are involved in all cases.

(Slide) This abdominal x-ray was taken of a 3-month-old infant 4 days before death from overwhelming staphylococcal pneumonitis. The marked ileus illustrated here is, in our experience, characteristic of a severe downhill course. It may mimic an acute intra-abdominal catastrophe.

(Slide) This 7½-year-old boy was struck in the nose by a football and developed a nasal septal abscess, orbital cellulitis, and meningitis due to the staphylococcus. On the fourth hospital day he developed a left tension pneumothorax and later that evening a right pneumothorax. At ten o'clock that night he developed cardiac arrest, which was treated with good recovery.

Eighteen days later he developed another tension pneumothorax. Following bouts of multiple pneumatoceles, this boy recovered completely. Because of the fulminating nature of these infections, the extensive destruction of pulmonary tissue, and a high mortality rate, especially in children less than 1 year of age, immediate antibacterial therapy is mandatory. While in the vast majority of cases a bacteriologic diagnosis and antibiotic sensitivities are easily arrived at by conventional methods, in those cases which present difficulty, lung puncture may be a valuable diagnostic aid.

DR. SABISTON (Closing).—In answer to Dr. Jensik's question, we have had only 1 patient who had a persistent pneumatocele which was troublesome. A catheter was placed into the pneumatocele and suction was applied for 48 hours with complete disappearance.

In closing, I would like to express my appreciation to Drs. Meade, Snyder, Seley, Moore, Jensik, and Watkins for their interesting contributions to the discussion.

SURGICAL TREATMENT OF PULMONARY COCCIDIOIDOMYCOSIS

A Ten-Year Study

Bert H. Cotton, M.D., Pasadena, Calif., and J. W. Birsner, M.D. (by invitation), Bakersfield, Calif.

THIS PAPER contains further observations on pulmonary coccidioidomycosis to supplement a preliminary report of 30 cases of surgical treatment presented before The American Association for Thoracic Surgery in 1950. The total number of cases in which there was surgical treatment has now grown to 144 (Table I).

TABLE I. 144 SURGICAL CASES

1. Cavities	
(a) Pneumonectomy	11
(b) Lobectomy	58
(c) Partial lobectomy	63
2. Coccidioidoma	12

Altogether 1,500 cases of proved pulmonary coccidioidomycosis have been analyzed, the patients coming from the southern part of the San Joaquin Valley, where the disease is endemic, and from neighboring Los Angeles County. All cases were confirmed by complement fixation tests and/or microscopic demonstration of spherules in sputum cultures, animal inoculations, and studies of surgical or autopsy material.

Arthrospores carried by dust seem to be responsible for the greatest number of infections in animal hosts. Evidence is now available* that the host may be sensitized by a small dose of arthrospores, as demonstrated by a positive skin test, and subsequently reinfected by exposure to a larger dose of arthrospores. The original infection is more likely to be followed by dissemination; reinfection, on the other hand, frequently leads to pulmonary granulomatous lesions with cavitation. Massive doses of spherules or endospores will also result in infection of the host as demonstrated by accidental percutaneous injection of pus from the lesion of another subject, and by the observation that the disease occasionally spreads during the acute phase from

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Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

*Butt, Edward M., and Biddle, Marjorie: Paper in preparation.

one lobe to another. These newer findings supersede the statements made in our earlier paper to the effect that arthrospores (chlamydospores) represent the only infective stage of the fungus, and that reinfection is unlikely.

TRACHEOBRONCHIAL MANIFESTATIONS

Since the arthrospores enter by the pulmonary portal, we proposed the hypothesis that, in the absence of radiologic findings, many attacks of acute tracheitis and bronchitis must be presumed to be tracheobronchial manifestations of coccidioidomycosis. By 1953, 100 patients had been bronchoscoped during the active phase of the pulmonary disease, and it was found that in the beginning coccidioidomycosis is primarily tracheobronchial in distribution. These findings were interesting from a diagnostic standpoint as well as in their correlation with the clinical course and changes in the roentgenogram. Endobronchial lesions present generalized redness and hyperemia of the mucous membrane, the degree of reaction corresponding to the severity of the bronchitis. In cases in which the roentgenogram demonstrated parenchymal involvement, we were able to observe, in the draining bronchus and adjacent areas, progression to submucosal infiltration, in some cases with pin-point superficial ulceration. Granulation, however, was rarely encountered. Retained thick tenacious mucus filled the bronchus and covered the ulcers. The mucus was white to brown and had a shiny or enamel-like appearance. Occasionally, mucopurulent secretion was seen to flow from a draining bronchus in an area of parenchymal involvement. All these patients gave a history of previous chronic bronchitis or other pulmonary disease. Upon reviewing the cases complicated by cavities, it was concluded that prior pulmonary infection is a predisposing factor in the development of a cavity or granuloma. Microscopic studies of material recovered from the smaller bronchi and bronchioles revealed masses of fungus growing in the lumen. The vegetation was most abundant and widespread during the early stage of the disease. Surgical treatment at this time would be disastrous since it might lead to dissemination before the host has developed immunity, and bronchopleural fistula with complicating empyema would almost certainly follow if lung tissue and bronchi are transected under these conditions. Bronchoscopic observations, furthermore, demonstrated that healing of the lesions was paralleled by disappearance of abnormal shadows in the roentgenogram.

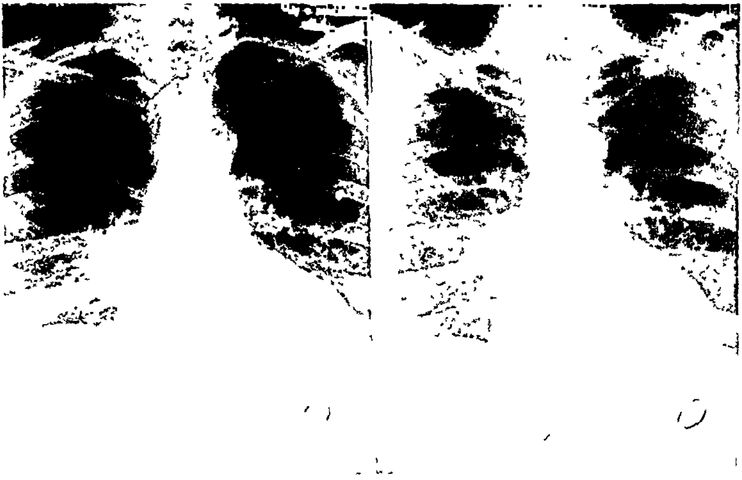
CAVITY FORMATION (Table II)

TABLE II. TYPES OF CAVITIES

I. Phantom "cavities"

II. True cavities
  1. Primary cavities—thin walled
    (a) infected
    (b) giant
    (c) cystic epithelized
  2. Secondary cavities—thick walled
    (a) caseous necrotic
    (b) fibrocaseous
    (c) cystic epithelized

Phantom "Cavities."—In our first paper on the subject, we discussed phantom "cavities" (Fig. 1) which are present during the acute phase of the disease, together with pulmonary infiltration, but which vanish as parenchymal involvement abates. It seems unlikely that such necrotic areas which are sometimes quite large and present the appearance of honeycombing and cavitation can disappear so rapidly without leaving a trace. In studying slides of the acute phase of the disease, we find that the fungus grows first in the bronchus, distending that structure by actual pressure or by means of a "check valve" mechanism. Then the mass is discharged via the bronchus, leaving a distended bronchus behind. Thus, an explanation is offered for the so-called phantom cavities, and we propose, therefore, to eliminate this category from the list of true cavities



A B

Fig 1—Large phantom cavity may be visualized in the right lower lobe associated with acute coccidioidomycosis X-ray studies 16 days later reveal the cavity to have disappeared and it did not recur

There are two types of true permanent cavities· primary, or early; and secondary, or late.

Primary Cavities (Fig 2).—Cavities of this type represent a different time phase and result in a distinct pathologic picture as compared with the secondary cavities They develop during the middle or late part of the infiltrative phase and are due to growth of fungi in the bronchi and bronchioles, distending these structures to the point at which they rupture and give rise to widespread necrosis. The debris is discharged via the bronchus and, in this way, a patent draining bronchus is established. Secondary b [illegible] terial invaders are then likely to penetrate through t [illegible] te to fi prepared bed in the necrotic tissues of the cavity. Under these circumstances, there develops what we have originally described as secondarily infected cavities. Since in most of these cases there exists a history of pre-existing infection, we feel that such a condition might predispose to more extensive tissue necrosis.

The further development may take one of two different courses. In the first, there usually remain secondarily infected cavities which may progress to become giant cavities. This was a frequent finding in the low-income group of field workers who did not report for follow-up treatment. Giant and infected cavities were discussed and listed in our earlier paper as requiring surgical removal since they are analogous to a pulmonary abscess. Pathologically these cases show collapsible cavities with patent draining bronchi. No "check valve" mechanism develops and they are therefore not likely to rupture. Eventually, dense adhesions are observed between the layers of the pleura. After long-standing necrosis or suppuration, lung tissue, like any other, shows few organisms of coccidioidomycosis. In these cavities, fungus growth may be encountered up to 6 months after infection but, at the end of 12 months, fungi are difficult to find and can sometimes not be demonstrated at all in the walls of the cavity.

In our report on the earlier series, we stated that 6 months after the original infection a cavity would be very unlikely to close spontaneously, and that, following a waiting period of at least 6 months, surgery might be advised. However, even after such a delay we still encountered minimal to moderate numbers of new generations of coccidioidules in the lung tissue adjacent to the cavity wall. The lack of a clearly demarcated cavity wall in these early cases caused us to resort to wide pulmonary resection as the safer procedure. On the basis of more recent pathologic findings, we now advise a waiting period of 12 months. Even though the secondary infection may still be rampant, the risk of dissemination is reduced because fungus growth is either minimal or has entirely ceased.

Primary cavities proceeding to reinfection by secondary organisms and to the stage of a giant cavity present the roentgenologic appearance of a thin-walled excavation which might be mistaken for an emphysematous bulla. A fluid level can rarely be demonstrated. Clinically important is the fact that cavities of this type are very likely to bleed. One of our patients died from hemoptysis due to a giant cavity.

The second course which the development of a primary cavity may take is encountered in subjects in the higher income groups, and patients who had received adequate treatment. Cases of this type are managed by repeated administration of specific drugs, to keep the cavity reasonably free from infection by secondary bacteria. The pocket will gradually be epithelized by bronchial mucosa and there develops a sac-like structure analogous to a congenital bronchial cyst. All that remains of the fungi are occasional spherules without endospores which are difficult to demonstrate.

The chest film shows a very thin-walled cyst which is difficult to visualize except with Lipiodol. One is often deceived into thinking that such a cavity

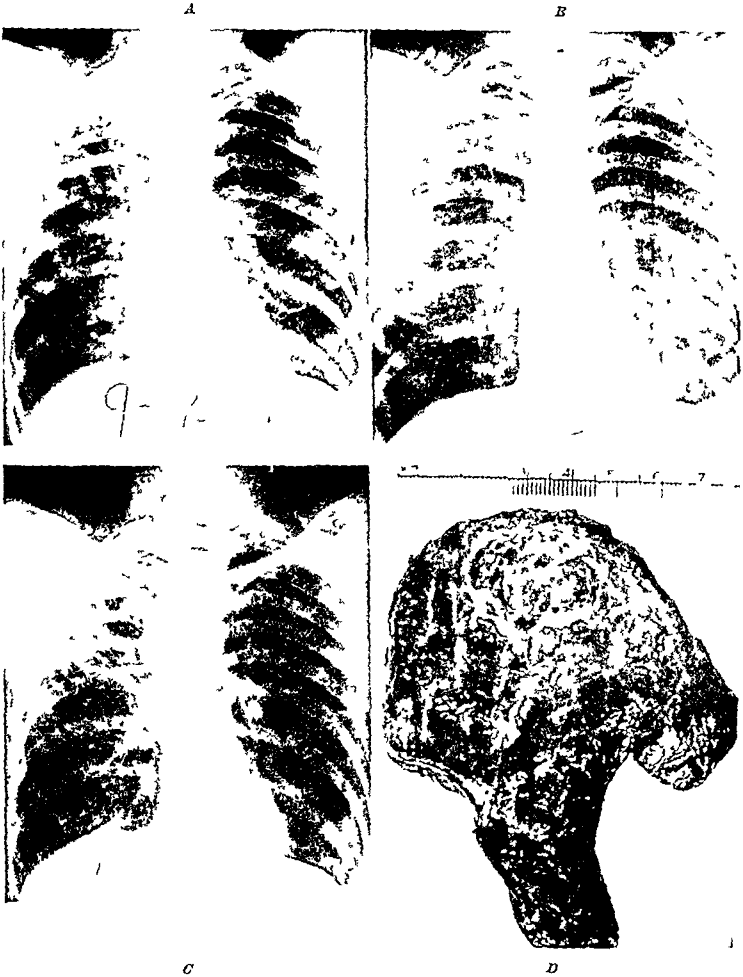
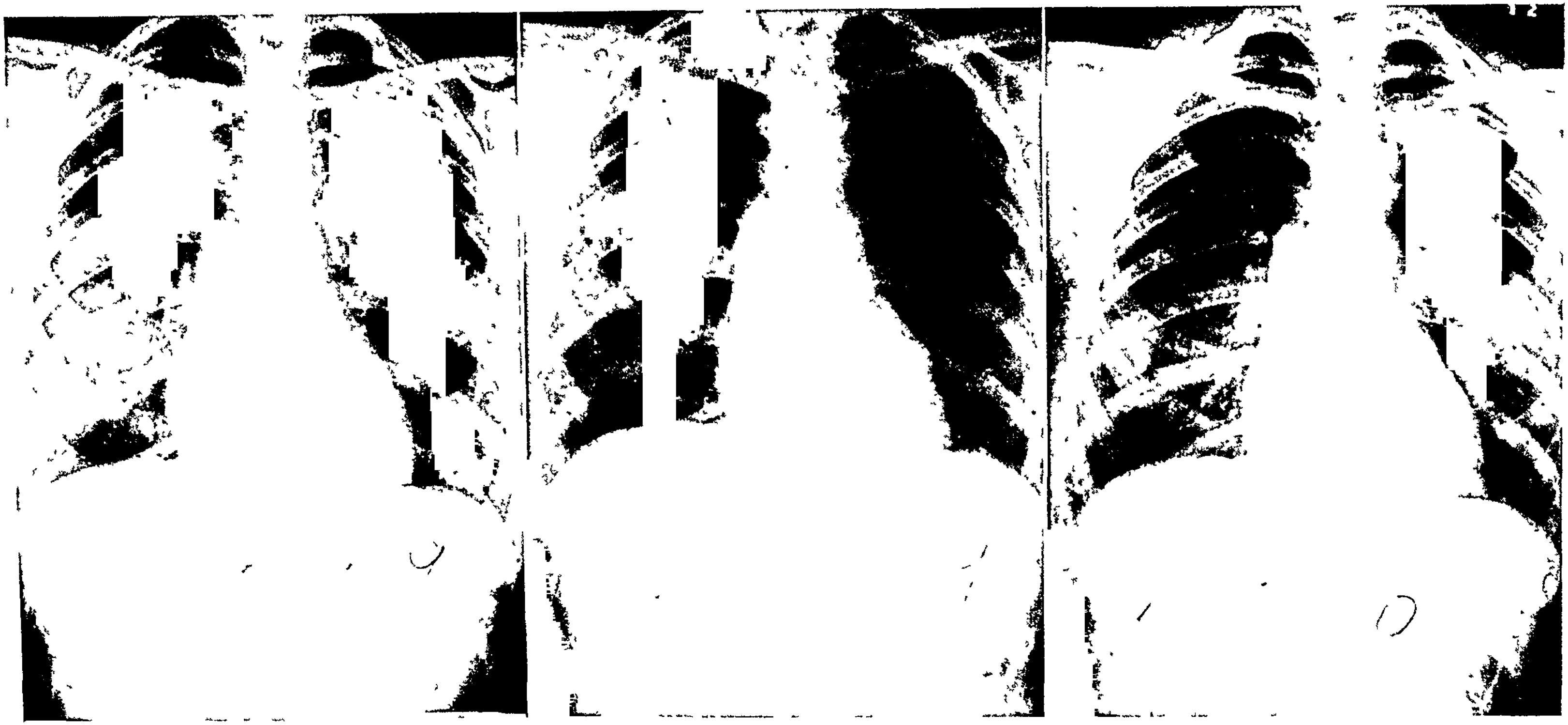


Fig 2 — A Primary cavity is seen in the right upper lobe associated with the acute phase of the disease

B, X ray studies 6 months later reveal the infiltration almost gone but the cavity is larger

C X ray studies 4 years later show a giant cavity of the right upper lobe

D Photograph of pathologic specimen reveals a comparatively thin walled cavity No necrotic membrane is seen



A. *B.* *C.*

Fig. 3.—A series of x-ray studies showing progression from an acute infection (*A*), to the formation of a granuloma (*B*), and secondary cavitation (*C*).

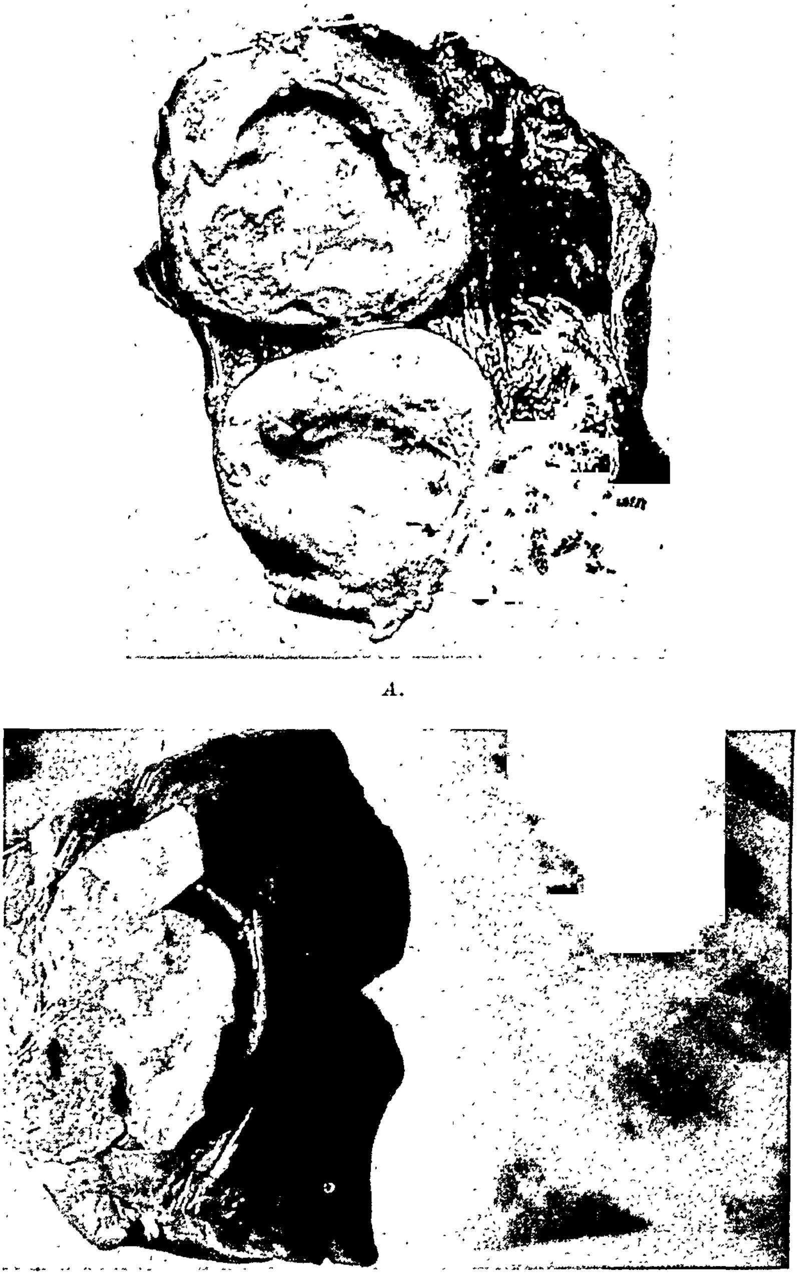
has disappeared because the patient is asymptomatic and cavities cannot be demonstrated radiologically However, there may be clinical and radiologic evidence with even a slight intercurrent infection

Primary cavities of this type are best treated by surgical removal and, since there are few organisms of *Coccidioides immitis* present, the danger of a postoperative complication is minimal or absent Personally, we have never encountered complications in such cases It may be possible to show that the incidence of postoperative complications varies with the types of coccidioidal cavities and with the extent of surgical excision This could well account for discrepancies in the literature with respect to complications and recurrences

Surgical intervention in the presence of such cavities will depend on whether one prefers to treat cysts operatively or expectantly In our experience, surgical removal of all cavities is indicated, otherwise, distressing complications and symptoms are bound to occur Even with the best medical management, one is only postponing the inevitable development of trouble weeks, months, or years later

Secondary Cavities—This second type of cavity develops by a different sequence of events Following primary infection, the infiltration gradually localizes but leaves a smoldering necrotic granuloma which subsequently may show cavitation (Fig 3) or become a true coccidioidoma The coccidioidal granuloma is a lesion rich in organisms, containing many gross and microscopic abscesses The latter are due to the growth of the organisms and cavitation by necrosis After cavitation, many gross and microscopic abscesses will be encountered in the lung tissue adjacent to the cavity At first, a heavy necrotic layer lines the cavity which later becomes fibronecrotic Such cavities, with a relatively thick wall and surrounded by only minimal parenchymal disease show characteristic shadows in the roentgenogram (Fig 4, *B*) Secondary cavities will not collapse, even with manual pressure Despite their benign appearance, which makes one think that they might be easily shelled out, such cavities are surrounded by secondary granulomatous coccidioidules of both gross and microscopic size which develop in the lung tissue adjacent to the cavity The fungus growth is heavy and one may see organisms characteristic of the parasitic phase as well as the mycelial form growing side by side Thus the only successful management is cautious, wide resection Late cavities are most likely to distend rapidly due to a "check valve" mechanism in which the heavy necrotic lining acts as a flap, and frequently a resulting fluid level can be demonstrated In our series, we encountered 8 cases of ruptured cavities The patients were treated by pulmonary resection and decortication in the presence of active coccidioidal empyema, and complete re expansion of the lung followed In all instances, the wound healed by first intention We feel that success in these cases was due to resistance of the host and elimination of most of the fungi by removal of the cavity together with the pleura, followed by immediate re expansion of the lung

Coccidioidoma.—The true coccidioidoma is a contracted solid fibrocaseous nodule in which spherules are rare or absent. Even repeated tissue cultures may not reveal any growth, and frequently the pathologic report is for granuloma, etiology undetermined. Radiographically such a solid tumor would appear as a coin lesion and, since 30 to 50 per cent of all coin lesions are malignant, this finding would become an absolute indication for surgical

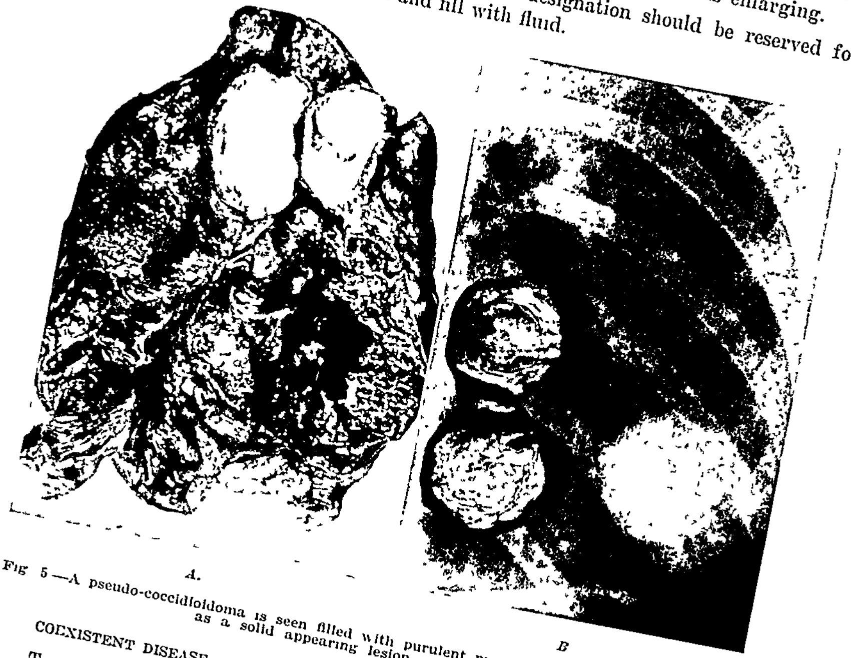

A.

B.

Fig. 4.—Two stages of secondary cavity formation. *A*, Beginning necrosis with cavity formation. *B*, Roentgenographic appearance of fully formed cavity.

removal. However, if the patient gives a history of having lived in a geographic area where the disease is endemic and if, in addition, the skin test is positive for coccidioidomycosis, the likelihood of malignant disease is no more than 2 per cent. Removal of such coin lesions is indicated only if they are 2 cm. or larger, or if serial films reveal that the lesion is enlarging.

Pseudo-coccidioidoma (Fig. 5).—This designation should be reserved for cavities which become blocked and fill with fluid.



A. B

Fig 5—A pseudo-coccidioidoma is seen filled with purulent material This cavity alternates as a solid appearing lesion and a cavity.

COEXISTENT DISEASE

Twenty-four cases of pulmonary coccidioidomycosis with coexistent tuberculosis have been observed. In this group, 9 adults were treated surgically and all have done well. The remaining 7 adults, as well as 8 infants and children, were treated medically. We have found that coccidioidal cavities secondarily infected by *Mycobacterium tuberculosis* are seldom amenable to collapse therapy. The treatment of choice is pulmonary resection.

Once a residual chronic cavity is well established, an infiltrative process is not to be regarded as an exacerbation of coccidioidomycosis, and a new etiologic agent must be sought. In our series, tuberculosis was the most common offender.

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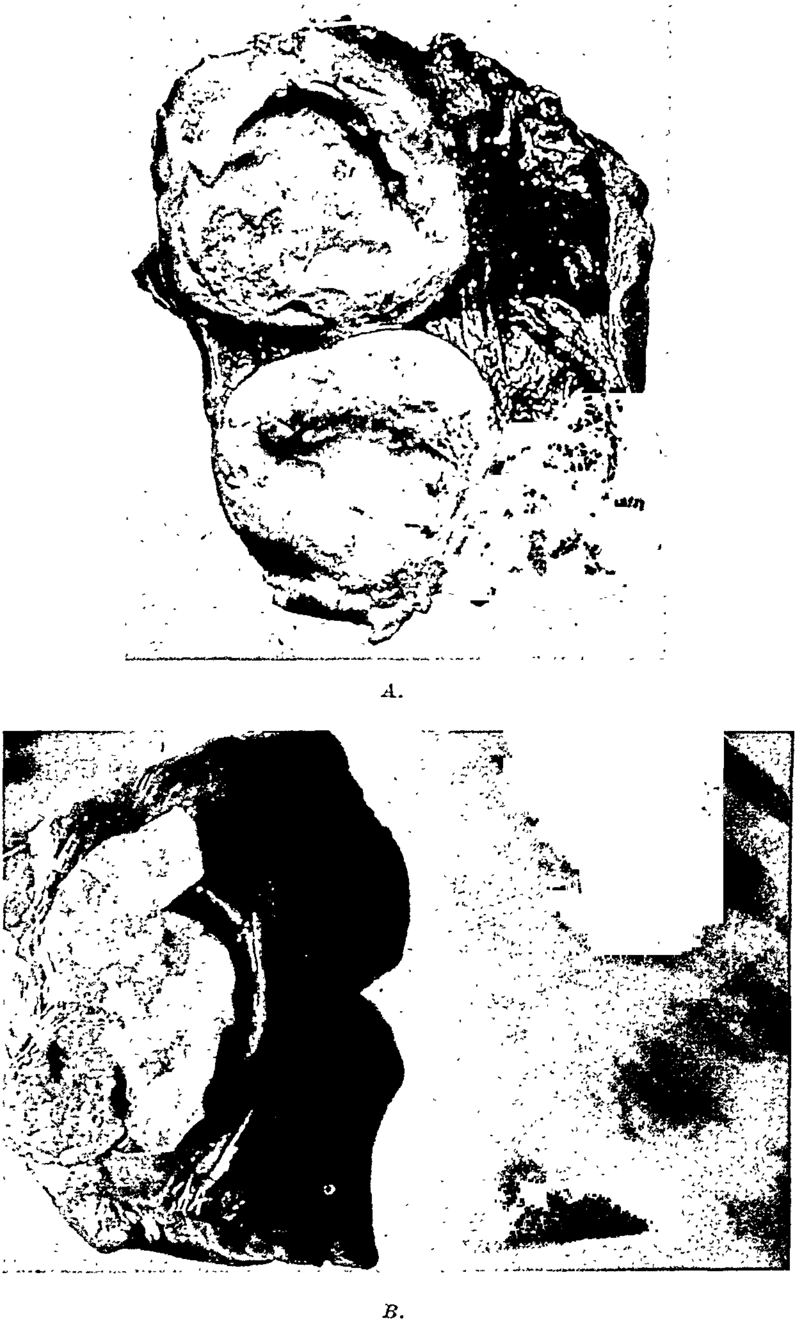

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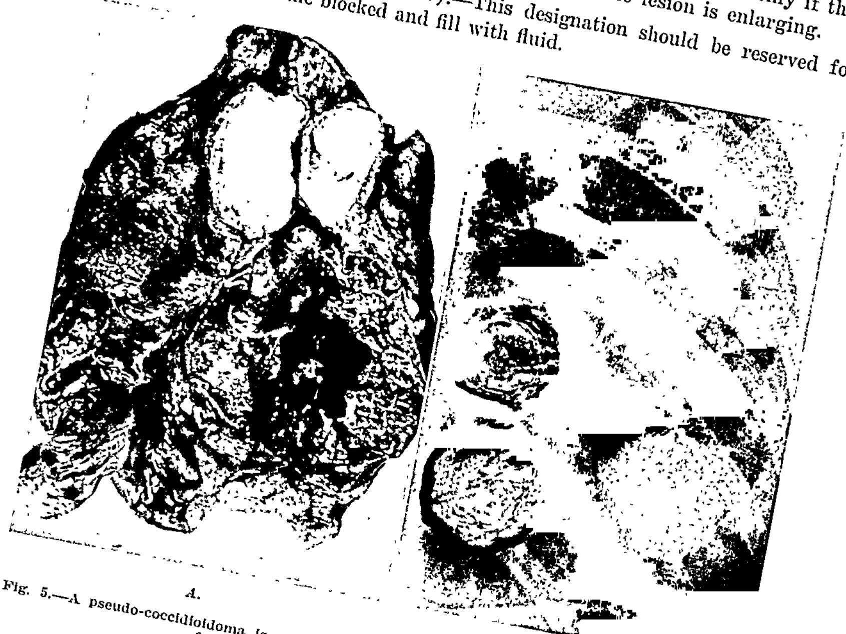

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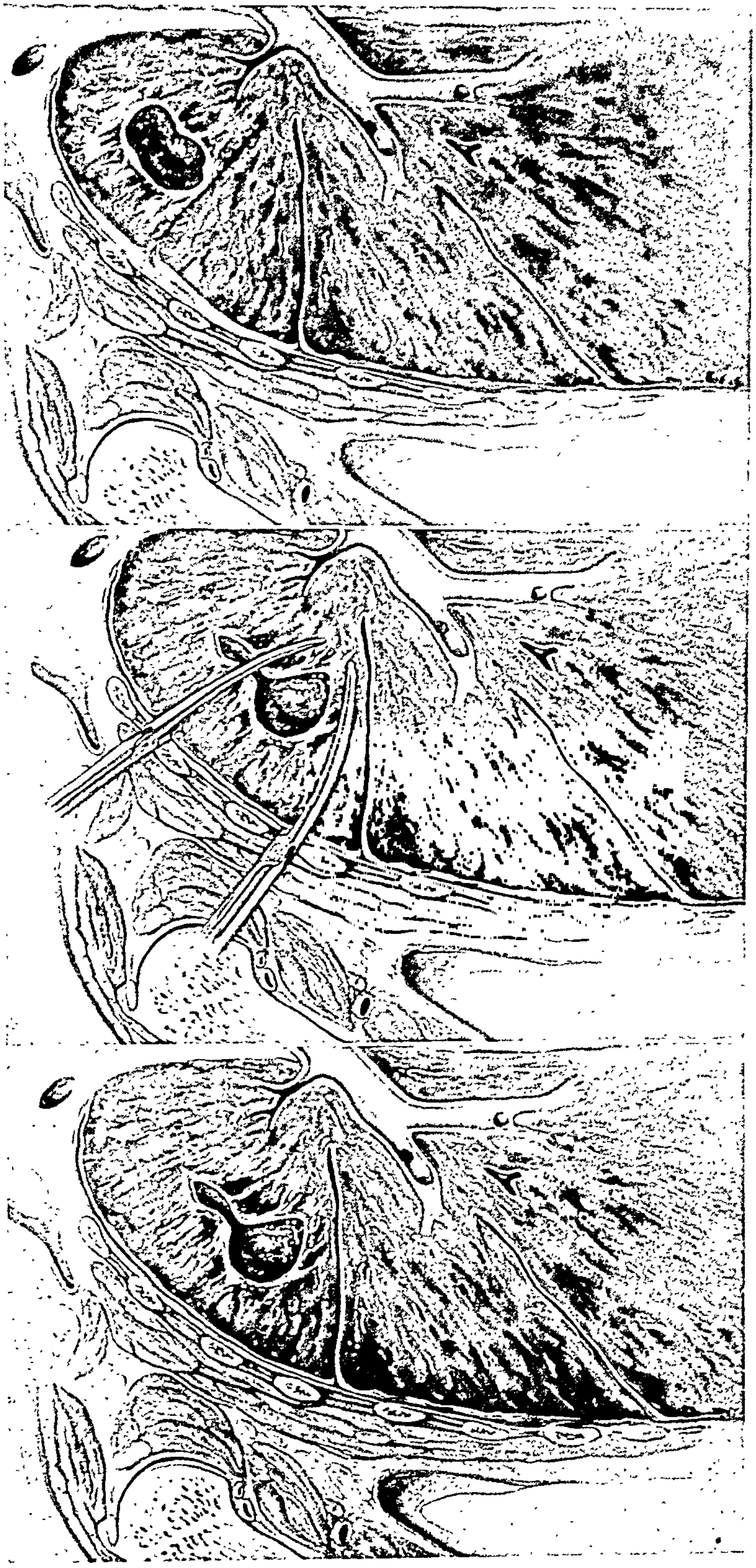

A. B. C.

Fig. 6.—A series of three pictures showing a possible cause of recurrent cavities. A small ramification of a cavity has been left in place during pulmonary resection.

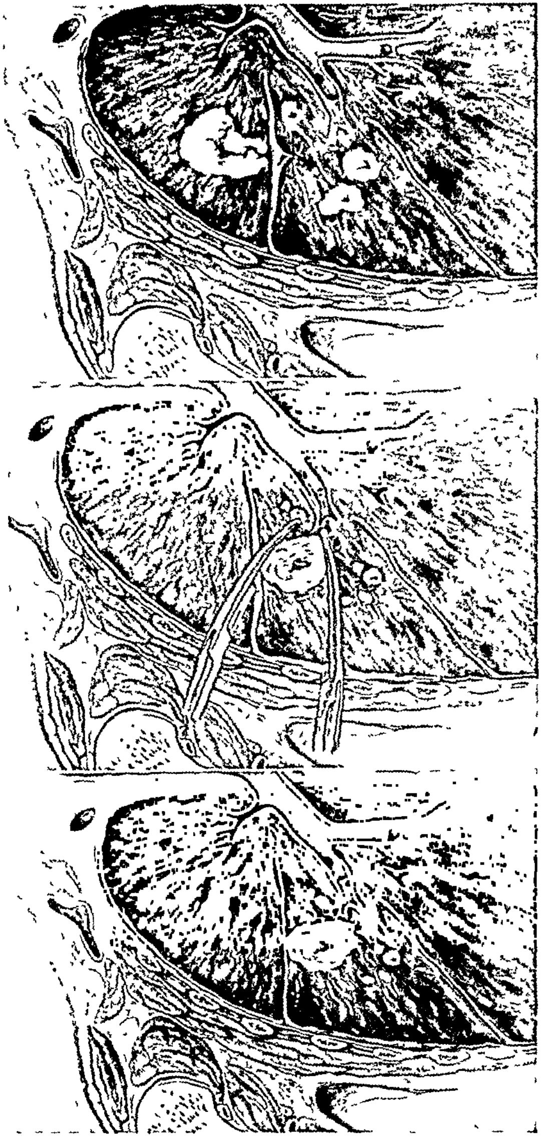

Fig 7 —A second cause of recurrent cavities may be the leaving behind of satellite coccidioidules or coccidioma during pulmonary resection Lesions kissing across the lobar fissure line may be the cause of the new lesions

Meningitis or pleural effusion appearing in a patient with a known coccidioidal cavity should be assumed to be tuberculous in origin.

Bronchogenic carcinoma is frequently difficult to diagnose in a geographic area with a high incidence of coccidioidomas, secondarily infected cavities, and unilateral hilar enlargement. Coexistent coccidioidomycosis and primary carcinoma of the lung were encountered six times in this series and 4 patients were operated upon. Carcinoma must be taken into consideration in the event that a nodular growth appears in the region of a previously resolving or stable lesion of pulmonary coccidioidomycosis, or when hilar adenopathy persists. In the lymphoma group, coccidioidomycosis develops frequently, but we have operated upon none of these patients, and most of them die of dissemination.

SURGICAL CONSIDERATIONS

In our earlier paper we presented the conclusion that operation is indicated without regard to the pathologic condition, or as to whether the disease is in a dormant or an active phase. Development of a postoperative secondary pulmonary cavity has caused us to revise our conclusions. We now believe that the surgical approach must be modified depending on whether fungi are present or absent. Since they are most abundant during the early stage of the disease, operative treatment should be avoided at this time due to potential complications, and especially since drug coverage is not available. Originally we thought that it would be safe to institute surgical treatment 6 months after infection, but we found that there was still heavy infiltration of the lesion with fungus. A waiting period of 12 months seems to be indicated. Since pulmonary coccidioidomycosis is primarily an endobronchial disease, associated bronchiectasis should always be suspected.

Primary thin-walled cavities result in less complications because of lighter infiltration by the fungus. In infected, giant, epithelized cavities, fungal involvement is minimal or absent. Lobectomy is indicated in the former group, and wedge resection in the latter.

The secondary thicker-walled cavities are more treacherous. Fungal infiltration is heavy, and we have discontinued segmental resection because of the greater likelihood of contamination. Lobectomy or wedge resection is indicated which must be wide, since the zone of involvement is always larger than the immediate area of the actual cavity. The roentgenographic appearance is deceiving, and one must avoid carrying the incision through satellite coccidioidules as this would predispose to a bronchopleural fistula. If there is any doubt as to the extent of the area to be excised, it is preferable to sacrifice a greater amount of lung tissue to avoid the risk of complications.

If a small ramification of a cavity (Fig. 6), a dilated bronchus, or satellite coccidioidules or coccidioidoma (Fig. 7) are left in place, a recurrent cavity may form. It will contain enough *Coccidioides immitis* to continue the parasitic growth cycle with probable cavitation.

RECURRENT CAVITIES

Recurrent cavities developed in 4 cases, 2 of which were reported in a previous paper. At that time, it was thought in one instance that the recurrent cavity and tuberculosis were coexistent but, after repeated reviews of the slides, it was concluded that the lesions were coccidioidules rather than tubercles. Recurrent cavities were detected 6 months, 2, 6, and 7 years postoperatively, all of them in the area of the previously resected cavity. Wedge resection had been performed in 3 patients. In the fourth case, no fissure line existed between the left upper lobe and the superior division of the lower lobe, and the recurrent cavity was situated in the apex of the lower lobe adjacent to the old cavity. On the basis of these findings, we now believe that a wedge resection may miss (1) a ramification of the cavity, (2) a dilated bronchus filled with fungus, and (3) one of the secondary coccidioidules. Moreover, a small isolated coccidioidal granuloma may develop a cavity in which the fungus continues to grow. Overexpansion of the lung or lowered resistance of the host may play some part in this development. Postoperative bronchopleural fistula or coccidioidal empyema were never encountered. All cavities with subsequent recurrence were of coccidioidal granuloma, or secondary, thick-walled type, and heavy fungus infiltration was present in all four original cavities. It is interesting to note that in one recurrent cavity mycelial forms were discovered, and that another was serologically positive after 7 years.

INDICATIONS FOR SURGICAL TREATMENT

The types of cavities of pulmonary coccidioidomycosis requiring surgical extirpation are explained by their equivalents (Table III).

TABLE III. SURGICAL INDICATIONS

TYPE OF CAVITY	EQUIVALENT
Phantom "cavity"	Reversible lesion
Primary	
Infected	Lung abscess
Giant	Destroyed lobe or lung
Cystic epithelized	Congenital cyst
Secondary	
Caseous necrotic	Tuberculous cavity
Fibrocaseous	"Healed" tuberculous cavity
Cystic epithelized	Epithelized tuberculous cavity

We believe that surgical removal of all primary and secondary cavities is indicated. Otherwise, many distressing complications and symptoms may develop. There is only one exception: a series of 124 children has been reviewed; in only 6 of these did the disease progress to cavitation. All the cavities closed before the end of 8 weeks except 1 which persisted into the chronic phase. On the basis of these findings, we feel justified in recommending prolonged observation of coccidioidal cavities in children.

As to the immediate operative course, all patients did well except 1 who died due to coronary occlusion.

TEN-YEAR FOLLOW-UP OF SURGICALLY TREATED CASES

Of the total of 144 surgically treated patients with pulmonary coccidioidomycosis, 58 could be followed over a sufficiently long period of time to render the findings significant. Recurrences or complications were observed in only four instances, and the remaining patients were free of disease. Symptoms were reported by 36 patients; in 29 of the cases they were slight and 7 patients described them as moderate. Symptoms consisted of light asthma, cough, shortness of breath on exertion, some white or yellow sputum and, in 1 case, there was heavy green and, in another, blood-tinged sputum. Twenty-two patients were completely asymptomatic. Forty-six patients evaluated their own physical status as ''good''; 1 reported a ''very good'' status; 10 considered their health as "fair"; and one as "poor." All of these patients were able to return to their former full-time work.

SUMMARY

1. This study is based on 1,500 cases of pulmonary coccidioidomycosis, confirmed by specific diagnostic methods.
2. Coccidioidomycosis is initially an endobronchial disease; the clinical, bronchoscopic, and radiologic findings during this stage are described.
3. Phantom ''cavities,'' which are not true cavities, may be encountered during the acute phase.
4. The true cavities are of two types: primary, or early, (thin-walled); and secondary, or late, (thick-walled).

DISCUSSION

DR. J. D. STEELE, San Fernando, Calif.—Dr. Cotton should be congratulated for his pioneer work in the surgery of coccidioidomycosis.

I was particularly interested in what he had to say about satellite lesions. We have been impressed with the necessity of wide excision of coccidioidal lesions, especially of cavitary lesions. We have found satellite lesions on careful pathologic examination of resected specimens in the vast majority of our cases. To be sure, satellite lesions are closer to granulomas than they are to cavities, and they may be widely distributed throughout the lobe in cavitary cases.

This slide shows an advancing case of coccidioidomycosis. Satellite lesions are seen scattered around the periphery of this lung tissue. This is an upper lobe and a superior segment resected for enlarging cavities. We did do a segmental resection in this case in preference to pneumonectomy. Possibly it would have been wiser to do a pneumonectomy because there are satellite lesions scattered through this superior segment.

This slide is a photomicrograph of another case in which there was a large cavity in the central portion of the upper lobe, and here is a satellite lesion far out toward the periphery of the lobe, so that we are fully convinced that in cavitary cases, except to avoid doing a pneumonectomy, a lobectomy is far preferable to a small resection.

DR. COTTON (Closing).—I wish to thank Dr. Steele for his comments.

I feel continued laboratory, clinical observation, and pharmacology research work are important to solve the many facets of this problem. Drs. Edward Butt and Marjorie Biddle are to be complimented on their splendid research work on coccidioidomycosis, with monkeys as the experimental subjects. A specific drug for this disease would be of great help.

THE EFFECT OF MEAN ENDOTRACHEAL PRESSURE ON THE CARDIAC OUTPUT OF PATIENTS UNDERGOING INTRATHORACIC OPERATIONS

Thomas F. Nealon, Jr., M.D., Richard T. Cathcart, M.D. (by invitation), William Fraimow, M.D. (by invitation), Edward D. McLaughlin, M.D. (by invitation), and John H. Gibbon, Jr., M.D., Philadelphia, Pa.

Anesthetized patients will frequently accumulate carbon dioxide in their blood and tissues if reliance is placed solely upon spontaneous respiration without help on the part of the anesthesiologist.[illegible] To prevent the accumulation of carbon dioxide and to ensure adequate oxygenation, the ventilation of such patients must be increased. The method of increasing ventilation most commonly used has been intermittent manual compression of the rebreathing bag, coincident with the inspiratory efforts of the patient. Mechanical devices have been developed either to assist the respiratory efforts of the patient or to take over completely the pulmonary ventilation.[13] Whatever kind of ventilation is provided the patient, care must be taken to avoid depression of the cardiac output by employing high mean endotracheal pressures.[illegible]

Earlier work from this laboratory[4] demonstrated an inverse relationship between mean endotracheal pressure and cardiac output of anesthetized patients undergoing abdominal operations. The following study was [illegible] to measure the effect of changes in endotracheal pressure on the cardiac output of patients undergoing intrathoracic operations.

METHOD

An endotracheal tube was inserted after anesthesia was [illegible]ed. The patient was then turned to a lateral position. Apnea was pro[illegible] by the intravenous injection of succinylcholine [illegible] during which pulmonary ventilation was provided by an automatic [illegible] negative pressure ventilator.* A ventilatory rate of [illegible] per minute [illegible] with approximately equal durations of inflation and deflation.

From The Jefferson Medical College and Hospital, Philadelphia, [illegible]

This work was supported in part by grants from the U. S. P[illegible] (H[illegible]) and Anthracite Miners Health and Welfare Fund.

Read at the Thirty-ninth Annual Meeting of The American [illegible] Surgery at Los Angeles, Calif., April [illegible]

*The Jefferson Ventilator [illegible]

The endotracheal pressure was continuously measured by a transducer attached to a tap at the end of the endotracheal tube. The pressure was visualized on an oscilloscope and photographically recorded. The pressure recording apparatus was recalibrated before each measurement of cardiac output. The mean endotracheal pressure was determined planimetrically from the pressure tracings in 7 patients. In the other 3 patients, the averages of the peak positive and negative pressures were taken to represent the mean endotracheal pressure. Because a negative pressure phase in the respiratory cycle has been reported to have no effect on cardiac output when the thorax is open,[1, 9, 10] the mean positive pressure during a respiratory cycle with the thorax open was estimated and taken to be one half of the inflation pressure.

A small polyethylene catheter was inserted percutaneously into the antecubital vein of the dependent arm and threaded up to the subclavian vein. The catheter was attached via a 19-gauge needle to a three-way stopcock and 5 per cent glucose in water was dripped slowly into the system to keep the catheter patent. A Cournand arterial needle was also inserted percutaneously into the brachial artery of the same arm. When not in use, the occluding stylet was left in place.

Cardiac output was measured as follows. Arterial blood was allowed to flow from the brachial artery via polyethylene tubing through a cuvette densitometer[8] and then into a collecting chamber under a constant negative pressure of 22 cm. of water. A solenoid valve inside this chamber permitted selective sampling of the blood without interrupting the flow. The dye curve was visualized on the oscilloscope and photographically recorded. A smooth base line was established at a constant rate of flow between 20 and 40 ml. per minute. With the camera in operation, a measured amount (approximately 5 mg.) of the blue dye, T-1824, was injected into the venous catheter followed immediately by a flush of 10 ml. of 5 per cent glucose in water. As the dye curve rose on the oscilloscope, the solenoid was activated to collect blood in a test tube within the collecting chamber. The period of collection of this blood was marked on the photographic record. The sample of arterial blood was centrifuged and the concentration of dye in the serum measured on a spectrophotometer. The cardiac output was then calculated from the measured concentration of dye in the serum and the planimetrically measured area below the inscribed curve during the period of sampling arterial blood.

Before the chest was opened, cardiac outputs were measured after maintaining the inflation and deflation pressures unchanged for at least 10 minutes. The pleura was then opened and the lung freed if pleural adhesions were present. Cardiac outputs were again measured after the inflation and deflation pressures had been maintained unchanged for 10 minutes. A change in cardiac output of 15 per cent or more from the preceding determination was regarded as significant.[3]

RESULTS

Ten patients were studied (Table I). The effect of changes in the mean endotracheal pressure on cardiac output was measured before the chest was opened in 8 cases In 5 of these, changes in the mean endotracheal pressure varying between 5 and 14 cm H_2O were accompanied by inverse changes in the cardiac output as previously reported In Case 2, the cardiac output rose 17 per cent when the mean endotracheal pressure was increased from +3 to +14 cm of water In the other case (No 5), the cardiac output steadily decreased before the thorax was opened, regardless of changes in endotracheal pressure In Case 7, there was only a 10 per cent decrease in output

The effect upon cardiac output of opening the thorax without changing the inflation and deflation pressures was observed in 7 cases (Nos 3, 4, 6, 7, 8, 9, 10) The cardiac output rose in 5 cases, the rise varying between +15 and +45 per cent There was a tendency for the increase in output to be greater when the mean endotracheal pressure was high In the other 2 cases (Nos 4 and 9), there was no significant change in output on opening the thorax

In the first 2 cases (Nos 1 and 2), the endotracheal pressure was high just before opening the thorax, and was low when the first cardiac output determination was made after opening the thorax In Case 1, with a change from a mean endotracheal pressure of +16 to +1, or to mean positive pressure of +9 cm H_2O, the output rose 80 per cent In Case 2, with a change from a mean endotracheal pressure of +14 to +1, or to mean positive pressure of +10, there was no significant change in cardiac output In Case 5, despite a rise in the inflation pressure of 5 cm H_2O, there was a significant increase in cardiac output on opening the thorax

The mean positive pressure was changed, and the cardiac output determined, while the chest was open, 12 times in 9 patients The change of 0 5 cm in mean positive pressure between the last two determinations in Case 7 was not considered significant In 5 patients (Nos 1, 2, 7, 9, 10), no significant effect on cardiac output was observed with changes in mean positive pressure of 6 5, 4, 3 5, 2 5, 2 5, 3 5, and 2 5 cm H_2O, respectively The changes in the mean endotracheal pressure were respectively 15, 9, 9, 6, 4, 9, 10, and 8 cm H_2O In 4 patients (Nos 3, 5, 6, 8), the same inverse relationship between cardiac output and mean pressure existed as in the closed chest The changes in mean positive pressure which resulted in significant changes in cardiac output in these 4 patients were 3, 2 5, 5, 5, and 5 cm H_2O, respectively The changes in mean endotracheal pressure in the same patients were, respectively, 8, 7, 13, 10, and 10 cm H_2O

DISCUSSION

In 6 of 8 patients, before the thorax was opened the same inverse relationship between cardiac output and mean endotracheal pressure was observed as had been reported previously in the course of abdominal operations Thus, it would appear that this relationship between endotracheal pressure and cardiac output with a closed thorax is unaffected by the change from the supine to the lateral position

Opening the thorax resulted in a significant increase in cardiac output in 5 of 7 patients In 4 of the 5 (Cases 3, 6, 7, 8), the mean endotracheal pressure

TABLE I.*

CASE NUMBER	AGE, SEX DIAGNOSIS OPERATION BODY SURFACE AREA	PULSE RATE	BLOOD PRESSURE		ENDOTRACHEAL PRESSURE		MEAN ENDO-TRACHEAL PRESSURE (CM. H_2O)	CARDIAC OUTPUT (L./MIN.)	CHANGE FROM PREVIOUS CARDIAC OUTPUT (PER CENT)
			SYSTOLIC (MM. HG)	DIASTOLIC (MM. HG)	INFLATION (CM. H_2O)	DEFLATION (CM. H_2O)			
1	74, Male	84	110	80	+16	-18	+ 3	4.3	
	Tuberculoma of right middle lobe	84	112	80	+16	-17	+ 2	4.2	N.S.C.†
	Excision		104	80	+30	+ 1	+16	3.1	-26
	2.16 $M.^2$		180	100	+17	-19	+ 1	5.5	+78
			160	90	+30	0	+16	5.8	N.S.C.
2	61, Male	92	110	70	+20	-13	+ 2	5.1	
	Fibrosarcoma of left chest wall	92	120	80	+19	-14	+ 3	4.8	N.S.C.
	and left lower lobe	92	110	70	+31	- 1	+14	5.6	+17
	Lobectomy and excision of chest	84	120	70	+20	-15	+ 1	6.0	N.S.C.
	wall	80	120	70	+28	- 3	+10	6.6	N.S.C.
	1.99 $M.^2$	86	120	70	+21	-16	+ 1	6.3	N.S.C.
3	51, Male	110	92	50	+17	-15	+ 1	4.7	
	Right upper and middle lobe	104	92	52	+26	0	+12	3.8	-19
	abscess	92	90	50	+26	0	+12	5.5	+45
	Bilobectomy	104	104	50	+20	-10	+ 4	7.0	+27
	1.79 $M.^2$	88	80	40	+25	0	+11	5.6	-20
4	65, Male	88	94		+20	0	+ 7	4.1	
	Carcinoma of left lung Pneumonectomy 1.86 $M.^2$	92	110	72	+20	0	+ 7	4.1	0
5	65, Male	74	118	60	+10	-10	0	5.9	
	Carcinoma of right lung	78	140	100	+30	0	+16	4.5	-24
	Exploratory thoracotomy	84	158	80	+15	-10	+ 2	3.2	-29
	1.54 $M.^2$	80	130	70	+20	-15	+ 3	3.7	+16
		80	110	70	+30	0	+16	2.6	-30

6	55, Male				+24	-10	+ 6	4.2	
	Tuberculosis of right upper lobe	102	126	80	+25	0	+11	3.2	-24
	Lobectomy	90	132	90	+25	0	+11	3.9	+22
	1 64 M.²	100	128	70	+15	-10	+ 1	5.0	+28
7	43, Male	88	120	76	+20	-13	+ 3	4.8	
	Osteogenic sarcoma of left chest	76	126	70	+21	0	+10	4.3	N.S.C.
	wall	94	130	70	+19	- 4	+ 9	4.9	+15
	Resection chest wall and portion	106	120	70	+14	-11	+ 3	4.6	N.S.C.
	of left upper lobe	100	116	80	+13	- 3	+ 7	4.5	N.S.C.
8	50, Female	90	160	110	+15	-10	+ 2	6.8	
	Middle lobe syndrome	90	170	110	+25	- 1	+12	2.6	-62
	Lobectomy	90	150	90	+25	- 1	+12	3.3	+27
	1.62 M.²	100	150	100	+15	-10	+ 2	5.3	+60
9	66, Male	90	132	90	+20	0	+ 9	3.0	
	Carcinoma of right lung	90	132	90	+15	-15	0	4.1	+37
	Exploratory thoracotomy	100	110	70	+15	-15	0	4.4	N.S.C.
		100	104	70	+20	0	+ 9	4.5	N.S.C.
10	60, Male	90	138	90	+10	- 8	+ 1	4.5	
	Carcinoma of left lung	78	148	90	+13	-13	0	5.0	N.S.C.
	Pneumonectomy	100	172	104	+13	-13	0	6.3	+26
	1.88 M.²	100	140	82	+20	0	+10	5.8	N.S.C.
		92	144	80	+15	-13	+ 2	5.2	N.S.C.

*The single horizontal lines between the data on each patient separate the cardiac output determinations with the chest closed from those with the chest open

†N S C indicates no significant change, i e, less than 15 per cent

before and after opening the thorax, the mean positive pressure after opening the thorax, and the peak inflation pressure were all high. It seems likely that, in these patients, opening the thorax improved cardiac filling and thus increased cardiac output. As the mean positive pressure and the mean endotracheal pressure remained high after opening the thorax, it does not seem likely that a change in the resistance to blood flow through the lungs could be responsible for the increased cardiac output.

With the thorax open, the changes in mean positive pressure were slight, ranging from 2.5 to 6.5 cm. H_2O, compared to the changes in mean endotracheal pressure, ranging from 5 to 14 cm. H_2O with the thorax closed. It is not surprising, therefore, to find that only 4 of 9 patients exhibited an inverse relationship between cardiac output and mean pressure with the chest open.

Humphreys and his associates,[11] many years ago, on the basis of animal experiments, came to the conclusion that the decrease in cardiac output with positive pressure inflation of the lungs in animals with an open thorax was "due to compression of the heart which hinders its filling rather than to compression of the pulmonary vessels which interferes with its emptying." Ankeney and his co-workers,[1] on the other hand, thought that the fall in cardiac output which occurred in the open chest with positive pressure insufflation of the lungs was due primarily to increased pulmonary vascular resistance. We are inclined to believe, on the basis of the data reported here, that the increase in cardiac output which we observed in some patients on opening the chest was due to the relief of the pressure on the venae cavae and right atrium when the mean endotracheal pressure was high. On the other hand, with the thorax open we believe that the decrease in cardiac output which occurred in some patients with an increase in the mean positive pressure was due to interference with blood flow through the pulmonary vessels.

Anesthesiologists and thoracic surgeons should realize that increasing the mean endotracheal pressure, or the mean positive pressure, during intrathoracic operations may produce a decline in cardiac output as it does when the thorax is intact. When the lungs are not diseased, the mean endotracheal pressure must be increased by 5 or 6 cm. of water when the thorax is opened to maintain expansion of the lungs. Any increase in mean endotracheal pressure above this slight amount necessary to keep the lungs expanded may result in a fall in cardiac output. Unnecessarily high endotracheal pressures can be most easily avoided by employing a mechanical ventilator in which the positive pressure phase can be easily regulated. The availability of a negative pressure phase to assist deflation of the lungs may be indispensable in the conduct of intrathoracic operations in patients with severe emphysema,[6] or crippling pulmonary disease.[12]

SUMMARY

1. The effect of changes in endotracheal pressure on cardiac output was measured in 10 patients undergoing thoracotomy, before and after the thorax was opened.

2 With the chest closed, the cardiac output tended to vary inversely as the mean endotracheal pressure

3 When the mean endotracheal pressure was high, opening the thorax resulted in a greater cardiac output

4 With the thorax open, slight increases in mean positive pressure resulted in a decreased cardiac output in 4 of 9 patients

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DISCUSSION

DR JAY L ANKENEY, Cleveland, Ohio —I would first like to congratulate Dr Nealon on this very interesting paper I, too, have been interested in this problem of cardiac output and endotracheal pressures before and after opening the thorax, the mean positive pressure after opening the thorax, and the peak inflation pressure were all high. It seems likely that, in these patients, opening the thorax improved cardiac filling and thus increased cardiac output. As the mean positive pressure and the mean endotracheal pressure remained high after opening the thorax, it does not seem likely that a change in the resistance to blood flow through the lungs could be responsible for the increased cardiac output.

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DISCUSSION

DR JAY L ANKENEY, Cleveland, Ohio—I would first like to congratulate Dr Nealon on this very interesting paper I, too, have been interested in this problem of cardiac output and endotracheal pressures

I think any study concerning the use of intermittent positive pressure ventilation and cardiac output should include detailed consideration of the pressure profile of the positive pressure machine used. Many years ago, Dr. Cournand showed in the closed chest that if the positive pressure occupied only one third of the respiratory cycle, there was no interference with blood flow. If the positive pressure phase was prolonged beyond 50 per cent of the cycle, cardiac output was reduced. Working in dogs in which we measured pulmonary blood flow continually, we found that this was also true in the open chest. Therefore, I wonder whether or not Dr. Nealon studied the pressure profile of his respirator, especially in those patients in which cardiac output was depressed. Perhaps the positive pressure phase occupied more than one third of the ventilatory cycle in these cases.

DR. GEORGE H. HUMPHREYS, New York, N. Y.—It is very interesting to hear a paper which goes back to some studies that we did 15 years ago, crude and rather primitive studies compared to modern methods, but nevertheless apparently confirming the work that was done on dogs in Dr. Miller's laboratory.

I wanted to ask the same question, essentially, that Dr. Ankeney has brought up; namely, when one speaks of mean pressures, it doesn't really tell us what the pressure relationship on the cardiac output is unless one knows the swing and the profile of the intermittent pressure relationship.

It seemed to us in our animal experiments many years ago, in which we used continuous pressure and maintained respiration by washing out the CO_2 with a catheter at the carina, that we could arrive at a continuous pressure which maintained respiration and which was optimal for cardiac output. Pressures above it and pressures below it both interfered with blood flow to the lung so far as we could tell.

I wondered if Dr. Gibbon's group had worked at all along those lines.

DR. H. F. RHEINLANDER, Boston, Mass.—We have been investigating cardiocirculating dynamics in patients during thoracic surgical procedures. Using cyclopropane anesthesia and a volume limited-pressure variable respirator, significant decreases in cardiac output and stroke volume occurred after the pleura was opened. The total peripheral resistance increased and the arterial blood pressure remained constant. Mean airway pressure, alveolar ventilation, pH, pCO_2, and blood cyclopropane levels were maintained at the closed chest levels.

Although a decrease in cardiac output and stroke volume is produced by surgical pneumothorax, under these conditions the circulatory regulatory mechanisms are intact and the arterial blood pressure is maintained as a result of the compensatory increase in total peripheral resistance.

DR. NEALON (Closing).—I want to thank the discussers for their remarks. I am fully aware that they have been interested in this problem for a long time.

Because of limitations of time I did not explain how we arrived at these mean pressures. There was a tap in the end of the endotracheal tube of these patients; by means of a transducer the endotracheal pressure was recorded on an oscilloscope and photographed. The mean endotracheal pressures were arrived at on the basis of a planimetric analysis of the inscribed curves.

The particular pressure pattern which we used is the one which is accomplished by the Jefferson ventilator. This has a roughly square pattern on both the positive and negative side. The duration of inflation was essentially the same duration as that of deflation.

I think that in the majority of instances the circulatory effects seemed to be related directly to the mean endotracheal pressure. A study we reported at this meeting 4 years ago showed that the greatest gas flow per pressure span could be accomplished with a duration of inflation essentially the same as the duration of deflation. Furthermore, this showed that the total volume of ventilation was directly related to the span between the peaks of inflation and deflation This points up one of the advantages of the negative phase, because if one increases the negative phase commensurate with the positive phase, *one can widen the pressure span to any limit without changing the mean endotracheal* pressure and consequently interfering little with the circulatory effects Using intermittent positive pressure, it is possible to increase the pressure span without increasing the mean pressure if the duration of inflation is decreased but there are limitations to this

We did not do any studies of various anesthetic agents Those reported were of patients who were induced with intravenous sodium Pentothal and some Anectine An endotracheal tube was inserted and anesthesia after that was nitrous oxide and oxygen

INJURIES OF THE TRACHEA AND MAJOR BRONCHI

R. Maurice Hood, M.D., Austin, Texas, and Herbert E. Sloan, M.D., Ann Arbor, Mich.***

Injuries of the trachea and major bronchi are occurring with increasing frequency. Still numerically uncommon, these injuries in the past have escaped early diagnosis. Surgical treatment has been instituted late and too often has not resulted in survival or adequate rehabilitation.

The present study has consisted of reviewing 91 cases reported in the present world literature and adding 7 cases of our own. The subject is approached from the standpoint of evaluating history and presenting findings and diagnostic procedures, in an effort to improve the ability to establish an early diagnosis. Surgical management of the early and late case is evaluated in the light of the 7 cases reported and those reviewed from the literature.

Kinsella and Johnstrud, in 1947, reviewed the literature regarding injuries of the tracheobronchial tree and were able to tabulate 38 cases and add 2 of their own. At that time there had been few correct clinical diagnoses and attempts at primary repair were not made in any case until then. Few patients survived and most of those who did developed a bronchial stricture which required resection.

Since that time, anesthetic and surgical techniques have changed considerably, so that, at present, successful primary repair of these injuries has become almost commonplace. It would seem obvious that bronchial or tracheal injuries should be diagnosed and repaired early. Most patients should survive and few should require pulmonary resection. A review of the subject at this time reveals, however, that there are still difficulties and delays in diagnosis and that resection is still used by many as an elective form of treatment.

Few surgeons have had extensive experience in this field, probably because such injuries are relatively infrequent. The majority of reported cases have been single case reports or, at most, 2 or 3 cases. Only Paulson, Ehrenhaft, Santy and associates, and Huizinga have reported a greater experience.

From the United States Naval Hospital, Oakland, Calif., and the University Hospital of the University of Michigan.

The opinions or assertions contained herein are those of the authors and are not to be construed as official or as necessarily reflecting the views of the Medical Department of the Navy or the Naval service at large.

Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

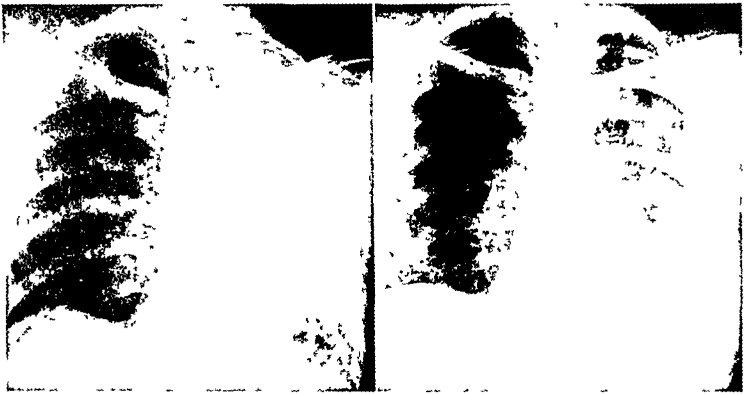
*Formerly, Commander, Medical Corps, U. S. Navy; Head, Thoracic and Cardiovascular Surgery Branch, Surgical Service, U. S. Naval Hospital, Oakland, Calif.

**Associate Professor of Surgery, University of Michigan, Ann Arbor, Mich.

CASE REPORTS

CASE 1.—J. W. M, a 42 year old white man, was involved in an automobile accident 5½ weeks before admission to the hospital. He had been hospitalized elsewhere with a partial left pneumothorax, pain in the chest, but no demonstrable rib fractures. An intercostal tube had been inserted into the left pleural space for management of the left pneumothorax, with immediate expansion of the left lung Following this, the hemithorax slowly became totally obscured. This was believed to be the result of a pleural effusion. However, in retrospect, it represented development of total atelectasis.

The patient, on admission, complained of a nonproductive cough with some anterior chest pain, moderate dyspnea, and slight orthopnea. He was not acutely ill. There was a marked shift of the mediastinal structures to the left side with shift of the trachea as well. Tactile and vocal fremitus were absent over the left chest and there was dullness to percussion over the entire left hemithorax. No breath sounds were audible over the left side of the chest.



A. B

Fig 1 —*A*, Roentgenogram (Case 1) made 5½ weeks after injury, demonstrating obscuration of the left hemithorax and retraction of the trachea and mediastinal structures to the affected side

B, Roentgenogram made 1 month following bronchial anastomosis There is still considerable pleural reaction which eventually cleared.

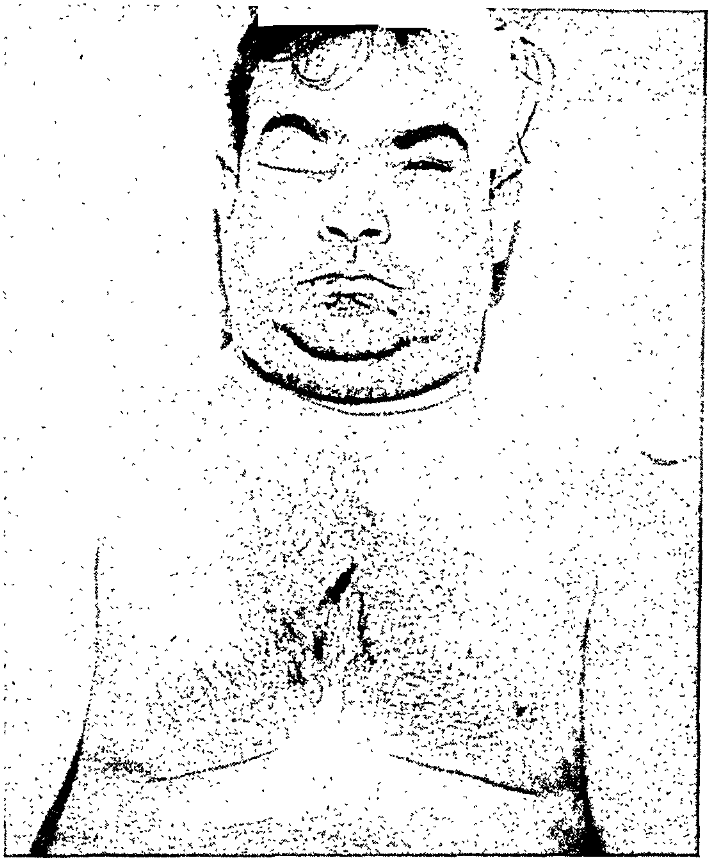
Chest roentgenograms revealed complete obscuration of the left hemithorax (Fig 1, *A*). There was retraction of the mediastinal structures and shift of the trachea to the left side. The right side of the thorax appeared normal. There was no evidence of rib fracture

On the day following admission, bronchoscopy showed a shift of the trachea to the left side and the left main bronchus terminated 2 to 3 cm. beyond the carina in a blind pouch. There was granulation in the central portion of the obstructed bronchus

A thoracotomy was performed 2 days later There was total atelectasis of the left lung with some straw colored fluid in the left pleural space There were a few adhesions between the lung and the chest wall. Exploration of the hilum revealed intact pulmonary vessels which were densely adherent to the bronchi The left main bronchus terminated 3 cm beyond the carina and was buried in an area of scar tissue There was a 2 cm gap between the proximal end of the bronchus and the distal bronchial stump which was also embedded in scar tissue The upper and lower bronchial stumps were mobilized and opened. The distal bronchial tree was filled with greenish, clear, mucoid material. This was aspirated as completely as possible and an end to end anastomosis was carried out using interrupted 4 0 silk sutures. On completion of the anastomosis, the left lung aerated well but it was necessary to aspirate the bronchial tree frequently in order to remove further mucous secretions. The chest was closed with drainage. The postoperative course was uneventful. Three weeks after operation, the main bronchus was found at bronchoscopy to have healed without stricture.

The patient was seen 5 weeks postoperatively and was found to be well. X-ray examination at that time revealed expansion of the left lung. There was still some pleural reaction (Fig. 1, *B*).

CASE 2.—P. D., a 27-year-old white man who was struck by the steering wheel of his car in an automobile accident, was admitted to the hospital. At the time of the accident the patient did not appear to be seriously injured but 12 hours later he noted swelling in the anterior portion of the neck, pain over the right anterior chest, and cough which was productive of bright red blood. The swelling increased rapidly after its onset and, on admission, involved all of the chest, arms, neck, and face.



A.

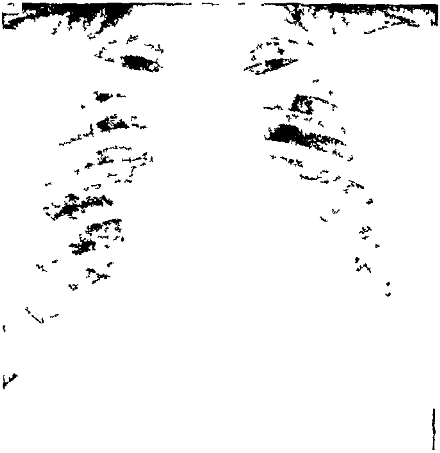
Fig. 2.—*A*, Photograph (Case 2) made shortly after admission, demonstrating the extent of emphysema.

At physical examination the patient was found to have a blood pressure of 122/72 mm. Hg and temperature of 101° F. There was marked subcutaneous emphysema involving the entire thorax, abdomen, head, and neck (Fig. 2, *A*). He had a cardiac rate of 128. Examination of the chest was inadequate because of the marked emphysema.

Admission x-ray studies demonstrated the emphysema and a left pneumothorax with 50 per cent collapse of the lung (Fig. 2, *B*). No evidence of fractures of the ribs or sternum was seen. A catheter was introduced through the second anterior interspace into the left pleural space, and connected to a water-seal system with suction. A large volume of air escaped, following which the left lung apparently expanded.

Emphysema persisted and increased further A repeat chest film showed an increase in interstitial emphysema but no pneumothorax Bronchoscopy was performed, revealing a transverse tear in the posterior wall of the trachea approximately 5 cm above the carina There was a mucosal injury over a much more extensive area and a flap of mucosa hung free in the lumen Air was evidently escaping through this defect The tracheobronchial tree otherwise appeared normal

Conservative management without surgical intervention was decided upon The emphysema decreased slowly and the lung remained expanded The patient was bronchoscoped 2 months later A small area of granulation at the site of injury was seen, without evidence of stricture formation or narrowing The patient was lost in follow up after this time



B

Fig 2—Cont d (Case 2) *B*, Roentgenogram made on admission which shows the partial pneumothorax on the left side and extensive interstitial emphysema.

CASE 3—M L P, a 24 year old white woman, was involved in an automobile accident She was hospitalized elsewhere and transferred to the University Hospital the same day

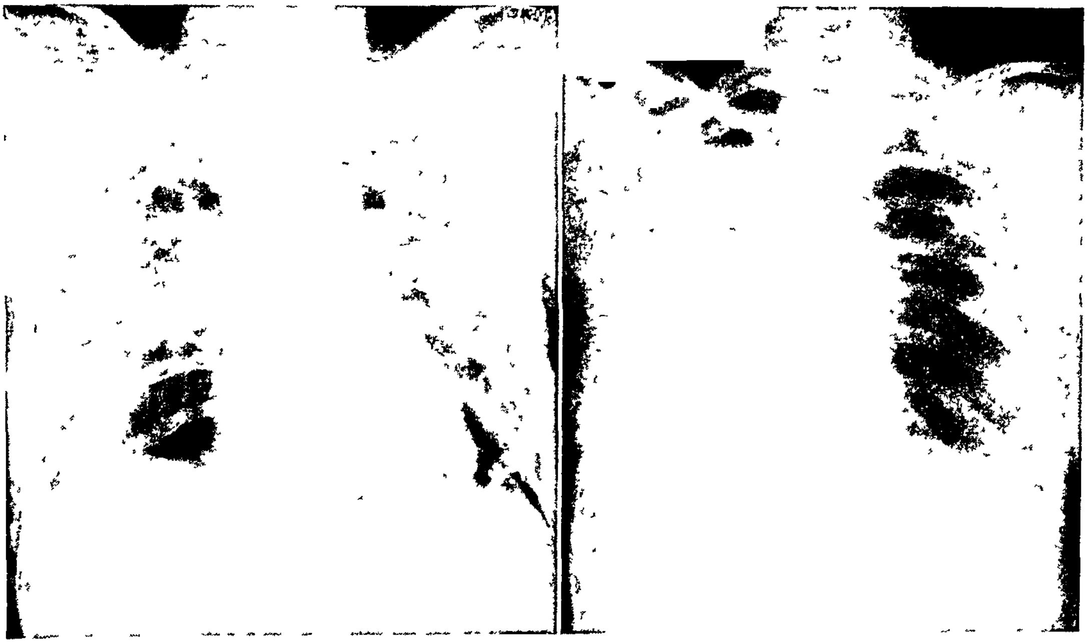
Physical examination upon admission showed a semicomatose woman who appeared to be acutely ill There were multiple facial bruises and lacerations There was marked subcutaneous emphysema which extended to the face and over the chest There was hyperresonance over the chest with decreased breath sounds, bilaterally Fractures of the distal third of the tibia and fibula and multiple bruises of the other extremities were present Neurological examination indicated only mild cerebral concussion

Chest x ray studies made upon admission confirmed the extensive subcutaneous emphysema and mediastinal emphysema There was bilateral pneumothorax with only minimal collapse (Fig 3, *A*) Chest films made 3 days later failed to visualize the previously diagnosed pneumothoraces

The patient developed a right hemiparesis and her mental state became confused for several days Difficulty was encountered in clearing bronchial secretions, and intratracheal suction was required on numerous occasions Two weeks following admission, a chest film showed a right pleural effusion and subcutaneous emphysema One week later, roentgenograms revealed multiple rib fractures on the right side, a pleural effusion with atelectasis of the right lower and middle lobes, and displacement of the trachea and mediastinal structures to the right (Fig 3, *B*)

Bronchoscopy, 4 weeks after admission, revealed a large amount of purulent material in the right main bronchus which was totally occluded 1 cm. distal to the right upper lobe orifice. This orifice could not be clearly seen. Repeated bronchoscopic dilatations were done over a period of approximately 1 month. A total of 24 endoscopic procedures were performed. After each bronchoscopy the stricture closed completely again.

Two months after admission, a right thoracotomy was performed and the stricture of the right main bronchus, just proximal to the right upper lobe bronchus, was found. The posterior wall of the main and intermediate bronchus was dissected free, incised, and a wire-supported, cutis graft was sutured in place. The lung expanded immediately and the postoperative course was uneventful.



A. B.

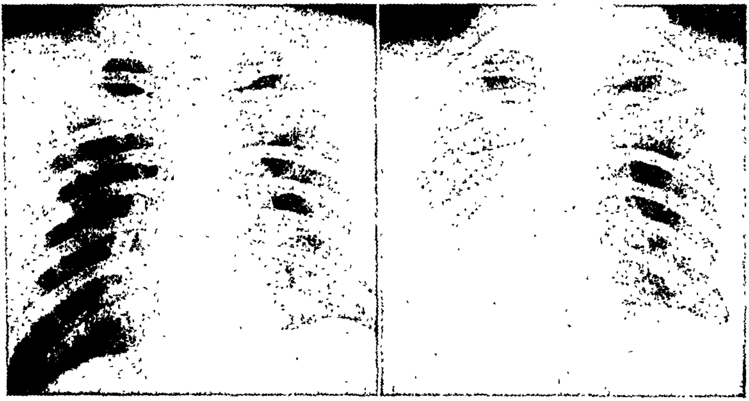
Fig 3—*A*, Roentgenogram (Case 3) made shortly after admission, demonstrating interstitial emphysema and a partial collapse of the right lung *B*, Roentgenogram made 3 weeks later, when the patient was supposedly recovering, showing the initial re-expansion had been followed by complete atelectasis.

Repeated bronchoscopic observations demonstrated that the area of the cutis graft was stricturing and 3 months later the wire support for the graft presented in the lumen and was removed. One month later the stricture had become complete. Reoperation was decided upon. At the time of operation, the area of previous repair was found to be heavily scarred and difficult to dissect free. At this time the entire area of stricture was resected and an end-to-end anastomosis was performed.

The course following this procedure was uneventful. Bronchoscopy on several occasions showed some irregularity and some narrowing of the bronchial lumen at this point but an adequate airway was maintained.

CASE 4. 21-year-old white man, received a crushing injury to the chest in an
bile was admitted to a local hospital in an unconscious state. At the
mination of the chest revealed no abnormalities with the exception
second ribs on the left side. He developed increasing evidence
g over the next 2 days, with retraction of the mediastinum
sferred 2 days after admission to another hospital. Be-
a tracheostomy was performed upon admission. An x-ray
some improvement. Bronchoscopy was performed and a

large amount of hemorrhagic mucopurulent material was aspirated from the left side. This was followed by clinical improvement and a lessening in the amount of atelectasis. X-ray examination 2 weeks later was considered normal. However, 4 weeks after injury he developed a tracheal wheeze. A bronchogram was performed, which demonstrated a stricture of the left main bronchus at the carina. Five days later bronchoscopy was again performed and the stricture of the left main-stem bronchus was seen. The patient was operated upon



A *B*.

Fig. 4.—*A* and *B*, Inspiration and expiration films (Case 4) made on admission to show *obstructive emphysema of the left lung and mediastinal shift on expiration. This patient was* found to have a secondary bronchial stricture following primary repair 4 months previously.

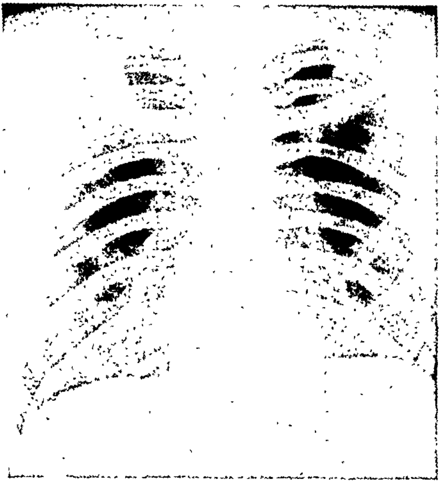


Fig. 5.—Roentgenogram (Case 4) taken postoperatively, following bronchoplastic procedure with a dermal graft. Expansion and function of the left lung were normal.

the same day and resection of the stricture with primary anastomosis was performed. The postoperative course was uneventful, except that it was found necessary to bronchoscope the patient repeatedly during the next 3 months, to cauterize granulation tissue at the point of suture. The patient was discharged finally with a stricture of approximately 50 per cent of the normal bronchial lumen. He was not seen subsequently until 2 months later, when he was seen at a Naval Air Station because of cough and intermittent wheezing on expiration. Physical examination at that time showed diminished to absent breath sounds on the left side. He was transferred to the U. S. Naval Hospital, Oakland, California, for further diagnostic measures and for therapy. On examination, the patient was found to have the physical findings described. Fluoroscopy revealed obstruction emphysema of the entire left lung with marked shift of the mediastinum to the right during expiration. Inspiration and expiration films confirmed this finding (Figs. 4, *A* and *B*). The patient was bronchoscoped and a severe stricture of the left main bronchus at the carina was identified with an opening estimated at less than 0.5 mm. This could not be dilated and tomograms revealed it to be a long area of stricture. The patient was subsequently operated upon and the stricture repaired by using a Gebauer type of wire-supported dermal graft.

The patient's postoperative course was uneventful. He was bronchoscoped, beginning approximately 1 week following operation, at weekly intervals for about 3 months. Granulation tissue appeared about the graft and several sutures were removed bronchoscopically. Granulation finally ceased and dilatations were not required from this point. The patient's pulmonary function tests following repair indicated about 50 per cent improvement over the preoperative studies. X-ray examination at this time showed the left lung to be expanded (Fig. 5). The patient was returned to full duty as an aviation cadet.

CASE 5.—R. A. S., a 22-year-old white man, was admitted to the U. S. Naval Hospital, Oakland, California, on Jan. 21, 1957, because of symptoms of bronchial asthma. He had severe bronchial asthma with evidence of infection, manifested by gross amounts of purulent sputum and fever. During the patient's hospital stay it was decided that bronchoscopy would be of value diagnostically and therapeutically. Therefore, he was bronchoscoped on February 21, under topical Pontocaine anesthesia. He was found to have suppurative bronchitis. During the examination of the left bronchial tree, the patient became excited and suddenly sat up with the bronchoscope in place. At the same time his head was sharply flexed on the chest wall. He was calmed down and, upon examination of the bronchial tree, a 1 cm. transverse laceration was seen on the medial wall of the left main bronchus which was bleeding moderately. Within 15 minutes of termination of the procedure, the patient had cervical emphysema which progressed to the point of producing emphysema of the entire head, neck, and anterior chest wall. No pneumothorax resulted and he subsequently recovered without any treatment.

Bronchoscopy 1 week later revealed a small area of granulation at the point of injury but no evidence of stenosis. The patient's subsequent course was uneventful, the asthma responding to medical therapy.

CASE 6.—E. P., a 22-year-old white woman, was admitted to the emergency room 1 hour following an automobile accident. She was not considered to be seriously injured. The injuries were found to consist of fractures of the pelvis, fractures of the right sixth and seventh ribs and the left fourth rib, and multiple contusions and abrasions.

A chest roentgenogram made the following day revealed the left hemithorax to be completely opacified, with retraction of the mediastinal structures to that side. Bronchoscopy and bronchograms revealed that the left main bronchus terminated 4 cm. from the carina in a blind sac. A history was then obtained that the patient had been involved in an automobile accident 7 years previously. At that time she had sustained fractures of 7 ribs on the left and a fracture of the clavicle. No pneumothorax or emphysema developed then. Chest films revealed the left hemithorax to have become opacified and were interpreted as showing a massive hemothorax. Bronchoscopy was not done. Following that injury, the patient had noted moderate dyspnea on exercise, which had not existed before the accident.

Thoracotomy was advised and refused initially, but was finally performed 5 months later. At operation, the left main bronchus was found to be disrupted with the proximal end encased in scar tissue and the distal end retracted 8 cm. inferiorly and similarly enclosed in scar tissue. The distal bronchial tree was filled with gelatinous mucus. The two ends were freed, débrided, and an end-to-end anastomosis was constructed, using 2-0 silk interrupted sutures. There was difficulty in removing the mucus from the bronchi and expansion was poor. There was considerable fibrosis of the left lung.

Postoperatively, partial expansion of the left lung occurred, but 6 weeks later bronchoscopy revealed stricturing of the anastomotic site. Since that time, repeated dilatations of the left main bronchus have been necessary to maintain any lumen at all. It is anticipated that plastic revision of the stricture or resection and re-anastomosis will be performed in the near future.

CASE 7.—W. H., a 19-year-old white man, was admitted to the hospital at 9:00 P.M., 30 minutes after being involved in an automobile head-on collision. He was the driver.

When first seen, the patient was semicomatose; the blood pressure was unobtainable. He was cyanotic and respiration was grunting in character. There was extensive and rapidly advancing emphysema of the chest, neck, and face. Physical examination indicated the presence of a tension pneumothorax on the right. This diagnosis was confirmed by thoracentesis. A No. 24 de Pezzer catheter was introduced into the pleural space through the right second anterior interspace and connected to a water-seal bottle with continuous suction of 15 cm. of water.

The patient's general condition improved dramatically. Cyanosis subsided, blood pressure rose to normal levels, and he became conscious and rational. However, over the next 6 hours, air continued to escape from the intercostal tube in large amounts. At times the air leak exceeded the capacity of the suction apparatus which was 5 L. per minute. A portable chest x-ray study indicated only 50 per cent expansion of the right lung.

Because of the continuation of an uncontrollable air leak and the inability to expand the right lung, a tentative diagnosis of rupture of a major bronchus was made and the patient was taken immediately to surgery. He was turned into the right lateral position and the chest rapidly opened. Exploration revealed a pneumothorax, and a collection of about 100 c.c. of blood in the pleural space. Upon each positive phase of respiration, large amounts of air were found to be issuing from a 0.5 cm. opening in the mediastinal pleura, just superior to the azygos vein. When this opening was tamponaded, the right lung could be expanded.

The mediastinal pleura was widely opened and the azygos vein ligated and divided. The exposure thus gained revealed that the right main bronchus had been completely avulsed from the trachea at the level of the carina and had retracted inferiorly about 5 cm. The intratracheal tube was advanced into the left main bronchus and the opening of the disrupted right main bronchus was occluded by the balloon. The torn edges of the trachea and bronchus were debrided carefully. The right main bronchus was then anastomosed to the trachea using interrupted suture of 4-0 cotton. An attempt was made to keep the suture extraluminal insofar as possible.

The postoperative condition of the patient was good and his course was uneventful. Bronchoscopy was performed on the third postoperative day, for the purpose of cleaning encrusted secretions from the suture line. An adequate lumen was present. Bronchoscopy was done again 6 weeks postoperatively, revealing at this time complete healing of the bronchus with a normal lumen. The patient was hospitalized for an additional 6 months because of a concurrent fracture of the femur.

DISCUSSION WITH REVIEW OF 98 CASES

Incidence.—Kinsella had been able to collect 39 cases at the time of his report. The 91 cases reported during the next 10 years reflect an increased awareness of the problem and a probable increase in the incidence of the injury.

The incidence according to sex indicates that males predominate in a ratio of over 3.1 (70 males to 21 females in 91 cases where the sex was stated). There was a marked predominance of individuals under 40, probably reflecting the fact that this age group is involved to a greater extent in hazardous occupations and includes those young people known to be prone to high velocity automobile accidents. Children who sustained bronchial injury, with only three exceptions, were those who were run over by some vehicle.

Types of Trauma Producing Bronchial Laceration and Associated Injuries.—In 84 cases, in which the cause of injury was recorded (Table I), 25 occurred in individuals riding in an automobile involved in an accident. Sixteen patients were crushed or compressed between or under objects; 13 were run over by the wheel of a vehicle; and 7 were struck by a motor vehicle. There were 6 patients who sustained their injuries from falls.

TABLE I. TYPE OF TRAUMA IN 84 CASES

TYPE OF TRAUMA	NO. OF CASES
Automobile collision	25
Crushed under or between objects	16
Run over by vehicle	13
Struck by vehicle	7
Penetrating wound	6
Fall	6
Endoscopy	4
Surgical trauma	2
Miscellaneous	5

Automobile accidents resulting in bronchial rupture appear to be the most common cause. However, when one compares the frequency of automobile accidents with the relative infrequency of other types of trauma producing bronchial injury, it is apparent that bronchial laceration is very rare among the total number of persons injured in automobile accidents. It appears that crushing or compression trauma is the specific etiology of most bronchial injuries and therefore is probably the mechanism in high velocity accidents rather than direct blows upon the chest.

Penetrating wounds are rare causes of tracheobronchial injury and only 4 have been recorded. This is further emphasized by referring to reports of chest trauma resulting from the Second World War by Mackler, Burbank and associates, Sanger, and Hanner and Cohen, which include only 5 instances of major airway trauma from literally thousands of chest injuries.

When the reported cases are studied with regard to other injuries concomitantly acquired, the selectivity of the injury and etiological trauma are emphasized (Table II). In 80 cases where this information was available, 42 patients were found to have sustained no other injury. Only 26 were reported to have had fractures of the bones of the thorax. Long bone and pelvic fractures were sustained in just 9 patients. Only 5 other patients had other major injuries. The cases of Ross, and Hughes and Fox are remarkable because of the presence of esophageal as well as tracheal injury resulting in tracheoesophageal fistula. Injuries to the spleen and liver are not reported; again marking the difference in trauma produced by compression and that produced by direct force These patients are in sharp contrast to those usually seen following automobile accidents in which chest injuries with multiple rib fractures are associated frequently with head injuries and multiple long bone fractures

TABLE II ASSOCIATED INJURIES IN 80 CASES

ASSOCIATED INJURIES	NO OF CASES
None	42
Fractures	
Bones of thorax	26
Pelvis	5
Long bones	4
Head injury	1
Injury of spinal cord	2
Esophageal rupture	2

Lesions—In this total series of cases, there were 18 injuries of the trachea Eighty bronchial injuries were recorded and all but 6 of these were in the main bronchi Forty one were on the right and 39 on the left The most common site of injury was within 1 or 2 cm of the carina although all individual lobar bronchi have been reported in the series Complete avulsion of the bronchus was the usual occurrence, although lesser injuries and, occasionally, linear tears occurred Cases 1, 4, 6, and 7 of this series are representative Only rarely, in contrast, was the trachea completely separated and the more common lesion here was a linear laceration Vascular injury, unless the trauma was of the penetrating variety, did not occur Intrabronchial and intrapleural bleeding were not infrequent but occurred in large amount in only 3 patients of the entire series It is felt that hemoptysis and bleeding into the pleural space in the majority of these cases have represented an injury to a bronchial artery rather than a pulmonary vessel An explanation of the exact mechanism of the avulsion of the bronchus by compression or shearing trauma without vascular injury is not obvious from the literature and no plausible theory is advanced in this discussion

The sequence of events occurring in the bronchus and lung distal to stenosis or occlusion is fairly well recognized For many years it has been recognized that high grade stricture formation, if allowed to persist, will result in secondary infection, bronchiectasis, and finally complete destruction of the involved area of lung Unfortunately, for many years this concept was thought to apply to complete bronchial occlusion as well as stenotic lesions The work of Crovatto and Lanari suggests that, from observations in the dog, complete occlusion of the bronchus by ligature will result in secretion of mucus into the bronchial tree to the point that bronchiectasis from this mechanism alone is the result It is apparently recognized that infection plays some part, although this is not clearly set forth in their article There are only 2 cases on record in which complete occlusion has been present and bronchiectasis or parenchymal damage has been reported

Complete severance which results in stricture formation is uncommon, having been noted in only 2 of the 98 cases reviewed Findings in our patients and in those reported in the literature suggest that when complete bronchial disruption occurs, each of the bronchial stumps, proximal and distal, heals by granulation and epithelization and the mucous glands continue their normal function until after lapse of time the bronchial tree becomes filled with mucus and somewhat dilated. This material remains sterile as a general rule. When the bronchus is filled to capacity and the pressure rises, mucus production is halted. Irreversible distention or bronchiectasis will not occur usually unless infection has complicated the situation. It is difficult to determine from the cases reported in the literature in which resection has been done whether bronchiectasis has been present or not. Studies of patients having primary repair after prolonged periods indicate that distention occurring with mucus production alone is reversible and that bronchiectasis does require infection for its production. The parenchyma does not appear to be damaged usually by having the bronchus occluded even for a prolonged period. The work of Mahaffey and his associates has demonstrated that reasonably good function can be expected even though the bronchus has been interrupted for a period as long as 12 years. However, Case 7 of this series suggests that, at least occasionally, intrapulmonary fibrosis may result in a situation in which the lung may not be sufficiently expandable to fill the thorax. Vascular shunting, demonstrated by Mahaffey, which occurs in prolonged atelectasis, is not altogether reversible and will impair the final functional result but apparently not to a serious degree.

Diagnosis and Diagnostic Procedures.—Table III is arranged to show the time interval from injury to diagnosis. In only 30 of the 90 cases, in which this information was available, was the diagnosis established in the first 24 hours. Eight additional patients were diagnosed by the end of 7 days and 15 others were recognized by the end of 1 month. There were 37 patients in whom the time elapsing before diagnosis was 1 month to 19 years.

TABLE III. INTERVAL FROM INJURY TO DIAGNOSIS IN 90 CASES

INTERVAL	NO. OF CASES	PER CENT
First 24 hours	30	33.3
1 to 7 days	8	8.8
7 to 30 days	15	16.6
30 days to 6 months	23	25.5
Over 6 months	12	13.3
Not made before death	2	2.2

These figures suggest that the diagnosis is not always readily apparent at the time of injury. Therefore, a review of the initial symptoms and findings immediately following injury (Table IV) discloses several facts which are remarkable. Pneumothorax, said to be present invariably, was identified in only 55 of 82 cases in which this information was recorded. Tension pneumothorax. which has also been said by several authors to be an almost constant finding, occurred in only 21 cases. Subcutaneous emphysema was present in just slightly over half of the patients. The remainder of the findings listed, although frequent, were not consistently present.

TABLE IV INITIAL SYMPTOMS AND FINDINGS IN 82 CASES

SYMPTOMS AND FINDINGS		NO OF CASES
Dyspnea		59
Pneumothorax		55
Open	2	
Tension	21	
Bilateral	4	
Subcutaneous emphysema		46
Cyanosis		24
Pain		20
Hemoptysis		18
Shock		14
Cough		8
Hemothorax		4

There were 8 cases in which no symptoms or only a cough or slight dyspnea indicated intrathoracic trauma. It is not surprising that many of these individuals have gone for prolonged periods before the correct diagnosis has been suspected.

When radiographic findings are considered, a similar situation prevails. The findings recorded may include pneumothorax which only occasionally has been under tension and in which the degree of pulmonary collapse has been partial or complete. With pleural intubation, expansion usually has occurred initially only to develop secondary atelectasis which has been either misdiagnosed as pleural fluid or has not been seen because of a failure to have follow-up x-ray studies. Hemothorax has been recorded but 4 times. Interstitial emphysema and rib fractures have been seen frequently but not always.

With regard to special diagnostic studies, there are just a few which appear to have been of value (Table V). Bronchoscopy was instrumental, as far as can be determined, in establishing the exact diagnosis more than any other procedure. Bronchoscopy was performed in 60 of 85 cases in which information was available and was listed as the procedure which proved the clinical diagnosis in 54 of the 85 patients. Bronchography was used in the late cases to demonstrate either bronchial strictures or termination of the bronchial stump and complete disruptions in 16 cases. It was the instrument of diagnosis in 9 of 85 cases. Planography was used occasionally and was listed as the means of diagnosis in only 1 case. In 16 of the 85 cases, no special procedure was utilized in diagnosis which was made on clinical impressions alone. This was true chiefly in the cases in which the patient's condition was one of extreme gravity and rapid diagnosis and treatment were imperative.

TABLE V METHOD OF DIAGNOSIS IN 85 CASES

METHOD	NO OF CASES
Bronchoscopy	54
Clinical	16
Bronchogram	9
Direct vision	[illegible]
Tomogram	[illegible]
Lipiodol swallow (tracheoesophageal f	[illegible]

How, in the face of nonspecific symptoms, physical and x-ray findings, can the diagnosis be established soon after injury? First, the history of compression or crushing injury to the chest should alert the physician. Second, a patient presenting with a pneumothorax which, when treated with an intrapleural catheter, is found to have a large, inexhaustible air leak should be considered to have major bronchial injury until disproved. Third, an individual with massive or rapidly advancing mediastinal or subcutaneous emphysema should be suspect. Finally, patients with these or less specific findings should not be allowed to escape clinical and radiographic observation until at least 2 weeks have elapsed following injury. X-ray studies made after this interval will almost certainly reveal the presence of tracheobronchial injury because of the developing atelectasis which will occur should it have escaped detection during the first 48 hours.

Bronchoscopy should be performed as soon as bronchial injury is suspected. There should be no hesitancy in repeating bronchoscopy if the findings are inconclusive or if clinical or x-ray findings remain consistent with bronchial injury. From the reported cases there are several instances in which the first bronchoscopy has not disclosed the injured area. Case 4 of this series was bronchoscoped on the third day following injury but the surgeon failed to discover the avulsed left main bronchus. This is not unexpected when one considers that bronchoscopy is being conducted under emergency conditions and the bronchial tree frequently contains blood which serves to obscure the expected laceration. The surgeon must exercise judgment about the extent of the diagnostic procedures permissible in the face of such an urgent situation. The diagnosis may have to be made and operative treatment planned with only clinical data for guidance, as was done in Case 6 of this series.

Diagnosis in the late post-injury period is not difficult as a rule. Complaints of the patient are usually those of dyspnea on exertion and occasionally cyanosis. This obtains if there has been complete occlusion of a major bronchus. A more unusual situation is that of a permanent stenosis of the trachea or major bronchus. In this situation there will usually be wheezing and a cough productive of purulent sputum, since bronchiectasis may have developed.

X-ray studies of patients with occlusion of a major bronchus characteristically show complete atelectasis of the involved lung with marked retraction of the mediastinum to the affected side. The chest wall may also show retraction and the diaphragm will be elevated. If the injury is to a lobar bronchus the findings will be of the same variety but less marked. If there is an incomplete disruption with stricture, bronchiectasis or lung abscess distal to the injury may be found. Occasionally, obstructive emphysema may be present if the area of stenosis is very small.

Bronchoscopy, bronchography, and planograms are very useful during the late post-injury period in confirming the clinical and x-ray diagnosis.

Management.—Treatment must be considered from several viewpoints, depending upon the condition of the patient, the presence of associated injuries.

the presenting symptoms and their early progress, and the availability of anesthesia for intrathoracic surgery, operating room facilities, and a surgeon capable of carrying out whatever corrective procedure is required

1 *Early management* This group of patients should include all of those so injured, however, experience has shown that only 33 per cent of the cases were even diagnosed in the first 24 hours

Some patients will present with clinical situations requiring immediate corrective attempts, rapidly performed, and preceded by minimal diagnostic procedures Occasionally, heroic steps to save the patient's life may be necessary Tension pneumothorax represents one of the true emergencies It should be managed first by insertion of a needle into the pleural space for the aspiration of air and replaced by an intercostal catheter with water seal suction drainage as soon as possible Rapidly advancing mediastinal emphysema may be controlled by such measures but, if progressive or if it is unassociated with a pneumothorax, may sometimes require an incision in the suprasternal fossa for the escape of air If the air leak is uncontrollable by these measures, bronchoscopy to establish the diagnosis should be followed by immediate thoracotomy, and direct suture or reanastomosis of the torn or avulsed trachea or bronchus

Airway obstruction may be acute because of intrabronchial bleeding and may be produced by a disruption of the trachea Tracheostomy and bronchoscopy may be vitally necessary even under admitting room conditions If the injury is tracheal and the airway cannot be assured, even by passing a cuffed intratracheal catheter beyond the point of injury, thoracotomy may be urgently required

Contrary to what one might expect, the situations described are not common and the patient may be expected to survive the first few hours without serious difficulty This is evidenced by the fact that there were but 7 deaths in the first 24 hours in the 98 cases reported, 8 patients required emergency tracheostomy and only 21 had tubes inserted for tension pneumothorax Only 4 of the 98 patients required urgent thoracotomy This, however, may be a misleading figure because there were other individuals who should have been operated upon early had the diagnosis been made

The presence of other serious injuries such as intracranial injuries and long bone fractures may require their taking precedence if the patient's respiratory status is not seriously impaired, even though the bronchial injury may be recognized Certainly experience has shown that delayed primary repair, although more difficult, may be expected to give good results

It is also suggested that thoracotomy be deferred, if possible, until adequate anesthetic and surgical facilities are available An emergency thoracotomy with inexperienced anesthetists or surgeons may unnecessarily cause the death of the patient when surgical intervention might well have been delayed Unfortunately this particular type of injured patient is not usually admitted to a medical center where management might be undertaken under ideal conditions

2. *Late management:* In this event the surgeon may examine the patient by any or all specialized techniques at his leisure and undertake definitive surgery with adequate preparation and planning. The type of procedure may be dictated by the location and extent of the injury, the condition of the lung distal to the point of injury, and will be influenced by the preference of the surgeon for one technique over another.

Techniques.—The following are described as the measures currently used, which may be of value.

1. *Primary suture or anastomosis:* Primary suture is without doubt the procedure of choice when possible. In the immediate period following injury this is easily done from a technical viewpoint, requiring only débridement and suture. The position of the patient requires comment. Exposure of the left main bronchus and carinal area from the left will be difficult when approached through an anterior or posterolateral incision. This difficulty is obviated almost completely by the prone position. Mobilization of the aortic arch may be required but is seldom necessary. Anesthesia must be temporarily administered by advancing the intratracheal tube into the opposite bronchus. The use of a double lumen tube such as the Carlen's tube is not of practical value in this type of procedure.

The suture material is a matter of personal preference. The authors prefer silk or cotton; however, stainless steel wire will serve well and is preferred by many. To prevent suture granulomata, Paulson suggests that sutures be kept extraluminal. Primary anastomosis after a delay of days, weeks, or months is much more difficult. There will be considerable scar tissue and inflammatory reaction in the area of injury. This may make the bronchial stumps difficult to identify. The freeing of the bronchus from the pulmonary artery may be tedious and hazardous. The prior encirclement of the main pulmonary artery by an umbilical tape will provide a margin of safety.

When the distal bronchus is opened, it will be found filled with a gray-green, clear, gelatinous mucus. As much as possible of this material should be removed by carefully aspirating all lobar and segmental bronchi prior to anastomosis. The area of suture should be buttressed by mediastinal tissue or pleura and must be airtight to positive pressure applied by the anesthetist before the chest is closed. The pleural space should be drained with two catheters connected to water-seal bottles.

Postoperatively, more difficulty than usual with bronchial secretions may be experienced. Complete expansion and clearing of focal areas of atelectasis may take several days. Bronchoscopy should be performed on about the third day to clear the sutured area of encrusted secretion. Later in the postoperative period, bronchoscopy is indicated to reveal beginning structure, as occurred in Cases 4 and 7 of the present series. This is usually produced by granulation along the suture line. Dilation and the removal of sutures bronchoscopically may be required. A note of caution also must be made against excessive endoscopic manipulation which may serve only to injure a healing bronchus.

2. *Dilation of strictures:* This procedure has been used as a method of choice in tracheal and bronchial tears when they have been recognized early. The results do not justify its use over primary repair. However, when the initial period has passed and a stricture has resulted from an incomplete laceration, dilation may serve to enlarge the lumen sufficiently. Numerous endoscopies over prolonged periods will be necessary and the technique may fail altogether. Case 3 of this series is an example in point. Unfortunately, when a stricture has existed for prolonged periods, bronchiectasis will have frequently developed and may require resection. The writers would prefer primary repair, resection of the stricture, and reanastomosis or bronchoplastic procedures rather than to resort to dilation.

3. *Bronchoplastic operations:* The classic work of Gebauer opened a new field in the correction of strictures of the tracheobronchial tree as a result of tuberculous bronchitis. The technique of wire supported, dermal graft has been proved by many surgeons to be effective when properly utilized. This technique has more recently been applied to stenoses resulting from injury. Two patients, Cases 2 and 4 of this series, were so managed. However, it is felt that with increasing experience primary repair or resection of the stricture with reanastomosis is preferable. First, bronchoplasty with dermal graft is technically more difficult, second, the final result is inferior to that obtained with direct repair. The technique of Ross in using a pedicled muscle graft to close a recurrent tracheoesophageal fistula may prove useful.

4. *Resection:* There has been an increasing realization that the lung distal to a ruptured bronchus with complete occlusion does not usually become infected and does not develop bronchiectasis. Thus, the incidence of primary resections for this entity has decreased. Nevertheless, there have been 24 resections since 1947 because of an occluded bronchus. It is apparent from a review of these case reports that only 2 were found to have bronchiectasis or parenchymal damage. It must be emphasized that resection, although technically the easiest solution to the problem, penalizes the patient by removing gross amounts of normal lung tissue, which is undesirable. Pneumonectomy has been the most commonly performed resection, and tends to produce a respiratory cripple. This situation in a young, otherwise healthy, individual is regrettable.

Results.—It is impossible to assess the results of forms of treatment statistically when the numbers treated are as small as they are in this series. Certain facts are obvious and other data are impressive enough to be conclusive. Table VI illustrates the methods used and classifies the results arbitrarily, according to the current authors impression of the original case reports. This means of evaluating results is not necessarily accurate. For example, a "good" result following primary repair is not comparable to a "good" result following pneumonectomy for the same lesion. From the data in Table VI it can be seen that not to treat patients with bronchial injuries is unlikely to result in complete rehabilitation and may result in the death of the patient. Also, dilatation of traumatic strictures, even in 6 cases, has been unsatisfactory. Of these, 3 show a "good" result but this figure does not take into consideration the long duration of therapy and the numerous endoscopic procedures required.

TABLE VI. METHODS AND RESULTS OF TREATMENT IN 95 CASES

METHOD	RESULTS			TOTAL
	GOOD	POOR	DEATH	
Primary repair	44	4	1	49
Resection	24			24
Bronchoplasty	3	1		4
Dilation of stricture	3	2	1	6
No treatment	8	4	7*	19

*Two of these died before any therapy could be instituted.

Resection has been shown to provide a satisfactory result if one is willing to ignore the respiratory loss that these patients sustain. Most resections were pneumonectomies which are particularly undesirable from the standpoint of postoperative function.

Primary repair is the obvious method best suited for immediate control of the injured bronchus, at the same time preserving maximal function.

Complications.—Complications have been exceptionally unusual in the reported cases and one wonders if those in the literature are reported because of the good result obtained and the less satisfactory ones were less likely to be published. In this series of 7 cases there were significant complications. The patient in Case 4 developed a high-grade stricture at the site of anastomosis 3 months after primary repair. This was managed successfully by utilizing a wire-supported dermal graft. Although the authors did not perform the initial operation there is no reason to suppose that this might be an unexpected complication. Stricture following anastomosis of any hollow viscus is a predictable complication. However, meticulous technique and prevention of infection and suture granulomata should minimize its frequency.

Case 7, at operation, was found to have extensive parenchymal fibrosis to the point that complete expansion could not be produced. The final result, therefore, was poor. This has been previously reported by Morichau-Beauchant in a case in which the lung had been atelectatic for 19 years.

The patient in Case 2 developed a complete stricture in spite of repeated dilatations and although the final result of delayed anastomosis was good, the folly of dilatation as a procedure of choice is demonstrated.

SUMMARY

Seven cases of injuries of the tracheobronchial tree have been reported. These have been considered with 91 from the literature reported since 1947. Certain facts and principles have emerged from this study:

1. Injuries to the trachea and the major bronchi are occurring with increasing frequency.
2. Compression or crushing chest trauma is the method of injury in the majority of cases.
3. Symptoms and signs may include subcutaneous emphysema, dyspnea, cyanosis, hemoptysis, pain, shock, and pneumothorax. These are not consistently present and may not be of sufficient degree of severity to arouse early suspicion.

4 Roentgenographic findings may be those related to pneumothorax but may be negative early Late roentgenograms will usually show complete atelectasis

5 Bronchial lacerations should be suspected from the type of trauma and when tension pneumothorax or subcutaneous emphysema are present A careful radiographic follow up for at least 2 weeks will disclose most injuries escaping earlier detection

6 Bronchoscopy will usually establish the diagnosis but may be supplemented by bronchography and planography

7 Immediate primary repair or anastomosis is the preferable treatment This is almost always technically feasible Delayed anastomosis, even though a period of weeks, months, or years has elapsed since the injury, will usually be successful The functional result obtained is also usually excellent

8 Resection is not preferred because a potentially functioning lung is removed which may result in serious respiratory insufficiency

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DISCUSSION

DR ROBERT R SHAW, Dallas, Texas—First I would like to congratulate Dr Hood and the other speakers of the day on the excellence of their presentations

Dr Hood and Dr Sloan have brought to our attention a condition that is being recognized more frequently, a condition which is life threatening and which, with prompt recognition and proper treatment, cannot only save a person's life but restore normal function

Dr. Paulson and I have seen, along with the residents under our supervision, 11 patients with tracheal tears and 6 patients with bronchial tears that have followed sharp, blunt blows to the chest Usually, as has been shown by Dr. Hood, these have not been associated by crushed chests or by multiple fractures of ribs

This slide is one of a patient treated by Dr E. S Crossett, of El Paso, during the time he was with us as a resident The patient was treated under the supervision of Dr. Paulson Dr Crossett quickly recognized the presence of a bronchial tear from the appearance of this first x ray Tracheotomy was done immediately Because the right lung could not be expanded and because there was rapid egress of air from the right pleural cavity, even with suction, the patient was anesthetized, turned into the prone position and (slide) the right thorax opened The next slide will show the type of tear that was found

This type of tear seems to show the shearing type of force that causes tracheal and bronchial lacerations Dr. Crossett was able to do a meticulous repair of the bronchus and restore complete function of the right lung. The patient was able to leave the hospital approximately a week following the injury

This slide shows a bizarre tracheal tear We have seen 11 tracheal tears Some of them have been lacerations that required only tracheostomies for control In this man's case, however, seen 1 year after the tracheal tear occurred, a tracheostomy had been put in place, but with difficulty it just barely kept the trachea open At first it was not recognized that he had sustained a tracheal tear, even though he had had massive hemoptyses for several days after the injury.

The diagram had to be touched up a bit because against the heart shadow it is difficult to show the tracheogram.

At surgery, a right thoracotomy was done. After the trachea had been dissected away from the surrounding structures, it was found that the tear had almost completely gone across the trachea about 3 cm. above the carina. Approximately one sixth of the circumference on the left side of the trachea had held. The major portion of the stenosis was really a crumpling of the trachea which, when it was fully dissected out, could be repaired. With freshening of the ends of the trachea, an end-to-end anastomosis with a very adequate lumen was accomplished.

This patient did have a complicating hemothorax which prolonged his convalescence, but he has since made a complete recovery and has a normal voice.

I again wish to express my appreciation to Dr. Hood and Dr. Sloan for this interesting paper.

DR. HARVEY W. KAUSEL, Albany, N. Y.—I, too, have enjoyed this presentation, and concur with the authors that the immediate treatment rarely requires major thoracotomy. The patients usually can be maintained with tracheotomy and catheter drainage if this is indicated, although occasionally, as Dr. Shaw pointed out, immediate thoracotomy certainly must be undertaken.

I should like to present a variant of this condition which was alluded to by the authors.

This slide is of a 21-year-old farm boy who ran into a telegraph pole and sustained an injury to his anterior chest; there were no other apparent injuries other than minor abrasions of the knee. He was hospitalized, and for reasons that are not clear was placed on penicillin for a period of 8 days. He was never kept in bed. Films of the chest, this one and others, revealed no evidence of fracture.

However, prior to discharge he complained of a cough. This film, which was taken at the time of admission, shows no fracture of rib, and a lateral film showed no sternal fracture. However, you will notice that there is subcutaneous emphysema in the cervical region.

(Slide) Despite the cough, the patient was allowed to go home and he was very recalcitrant to further investigation or treatment, and only after 6 months had passed did he return for medical assistance with a chronic productive cough and a weight loss of 40 pounds. A plane film of the chest reveals rather marked dilatation of the stomach; no other appreciable abnormalities. The cough was always precipitated by deglutition, particularly fluids.

(Slide) At esophagoscopy a fistula could be readily seen and a ureteral catheter was passed down the esophagus into the stomach and another smaller one through the fistula, and you can see it residing in the left lower lobe bronchus.

(Slide) The patient was explored. There was marked reaction around the esophagus and the membranous trachea was so thickened that it was possible to close this with two layers of silk. The esophagus was closed in a routine manner and a flap of parietal pleura placed between the two suture lines, which we think is very important, where two suture lines might abut, because of recurrence.

The mechanism of this injury is not completely understood. We feel that probably the cartilaginous rings are straightened out by abutting on the vertebral body, lacerating the membranous portion of the trachea, and then the cartilages snap back and they pick up the esophagus and perhaps cause this laceration.

DR. RICHARD M. PETERS, Chapel Hill, N. C.—We have been interested in two aspects of this lesion; namely, the mechanism of injury and some of the late results of chronic atelectasis. If the mechanism of injury is due to a shearing force it should be common in high-speed accidents. It is actually more common following crushing injuries, as pointed out by Dr. Hood. We postulate that the crushing force acutely increases the pressure in the trachea by compressing the air. According to Laplace's Law, the tension in the wall is directly proportional to the radius of the vessel. This fact would explain why injuries of the trachea and major bronchi are most common Ruptured bronchi when seen in the acute stage are not neatly sheared but have stellate tears. This type of injury further supports the concept of blowout

We also are interested in the late results of chronic atelectasis and why these patients do so well even without operative repair.

This slide shows an angiogram of a dog which had its bronchus transected when it was a puppy. The angiogram shows that there is virtually no circulation in the right lung in this dog The next slide demonstrates another angiogram after the bronchus was repaired The repair was not done until the dog was 2 years old. There is now some circulation in the lower lobe region on the right although if this angiogram is analyzed carefully you will see that most of the circulation comes from the good lung

This slide shows the autopsy specimens The lower one is the lung that did not have a transected bronchus; the upper one is the total lung on the other side, demonstrating that the lung does not grow if there is no ventilation but is less than one quarter the size of the control

I think it is important to point out that we all advocate repair in these circumstances, but there are very few reported oxygen saturation studies, particularly with 100 per cent oxygen, to be sure there is no significant shunt in these patients after repair. We should still have reservations about how much improvement we are giving the patients with chronic atelectasis.

DR EDOUARD D GAGNON, Montreal, Quebec—I enjoyed this paper very much. It was beautifully presented and so well illustrated

I would like to restrict my comments to the mechanism of injury. The previous discusser mentioned something in this respect. We have been working on this problem, and have recently reported this work to the Royal College of Surgeons in Canada. It will be published shortly

I think that we are dealing with two problems I have always been confused trying to decide the difference in the clinical picture between a complete rupture and a partial rupture I believe that some of the slides shown today, where the bronchus is completely torn across, especially the one by Dr Shaw, are probably the result of a shearing force, but when there has been a partial tear, whether in the trachea, the main bronchus or the smaller bronchi, it is a "blowout"

We all know the Zeuch theory Macklin, in 1937, who was then Professor of Histology in London, Ontario, carried out some very interesting work in the bronchi of cats, placing a catheter in the lower lobe bronchus and injecting air He described and published at that time, and again in 1938 and 1939, some pathways that the air followed after rupture or blowout of the smaller bronchi, the air creeping back along the vascular coverings of the bronchial tree back toward the mediastinum

We repeated this work, but with a cuffed tube, and found that the air not only came out of the bronchus and crept along the blood vessels, but also dissected backward along the bronchi I think that in partial tears, due to the increase in pressure and a closed epiglottis, there is a blowout or partial tear This would explain the clinical picture presented by the authors of a man who, 18 hours after injury (and remember he had hemoptysis in between his injury and the clinical picture) becomes a "puff ball man" as described in the literature

The *late* "puff ball man" is probably due to this creeping back of air along the bronchial coverings

I would like to know what the authors think about this mechanism of injury.

DR HOOD (Closing)—I would like to thank the discussants for their comments and for adding to this problem

The problem mentioned of tracheal esophageal fistula is an unusual problem. There have been only 8 cases reported in the literature up to now in which this has been a result of this type of trauma I think the operator in this case was fortunate to secure a primary repair without difficulty

This particular lesion in adults has had a notorious incidence of recurrence, and I think in this particular situation that the type of repair, as suggested first by Brantigan and later by Ross, is of value. This consists of interposing a pedicled muscle graft from the chest wall to separate these two suture lines.

The problem of shunting in prolonged atelectasis is well known. Two of our patients and the 1 reported by Mahaffey, which are the only ones in whom careful measurement of pulmonary ventilatory function has been done, have shown relatively normal values. Measurements have shown that the shunts have been relatively small. None of these patients has been cyanotic. I think perhaps if these had been injured in childhood the lung might not have grown, the vasculature of the lung might not have developed. But I think with the injury sustained in adulthood there will be little detraction from the final function. At least this has been our experience.

So far as the mechanism of injury, we have no plausible theory to suggest the exact mechanism of a rupture of the bronchus, although we are of the opinion that it is a shearing trauma. If it were a matter of pressure increase, I would think that the cartilaginous portion of the bronchus would remain intact. Perhaps the membranous part might rupture but not the thicker part.

Also, I would think that if this were the case there would be vascular injury on occasion—rupture of the great vessels, pulmonary vessels, or pulmonary veins. This has not been reported.

Furthermore, we are all familiar with the children who have had excessive endotracheal pressure applied in surgery, in attempting to expand lungs, and of course the only thing that ever ruptures is the alveolar areas of the lung. I don't believe—at least this is my opinion—that intrabronchial pressure increase is responsible for many of these injuries.

ADVERSE SURGICAL EXPERIENCE IN THE TREATMENT OF PULMONARY DISEASE CAUSED BY ATYPICAL ACID-FAST BACILLI

Robert W. Harrison, M.D. (by invitation), Arthur F. Reimann, M.D.** (by invitation), Edwin T. Long, M.D.** (by invitation), William Lester, Jr., M.D.** (by invitation), and William E. Adams, M.D.,* Hinsdale and Chicago, Ill.*

INTRODUCTION

Numerous reports in the literature describe the isolation of "atypical" acid-fast organisms from the sputum, gastric washings, or pleural fluid of patients with pulmonary disease simulating tuberculosis.[1-28] Among these atypical organisms were recognized various strains which became known as photochromogenic bacilli, "chromogenic" bacilli, nonphotochromogenic bacilli, "yellow" acid-fast bacilli, etc. Initially much uncertainty existed as to the relationship of these various atypical acid-fast organisms to human pulmonary disease. Many of these atypical bacilli were considered nonpathogenic on the basis of their inability to produce lesions in the guinea pig and were regarded as saprophytes. More recently the use of improved and reliable bacteriologic techniques has led to increased recognition of the role of atypical acid-fast bacilli in human pulmonary disease. Classification of the atypical strains into more or less well-defined groups has assisted in a clarification of this role. The first major groups of atypical organisms to be recognized on the basis of culture characteristics were the photochromogenic, nonphotochromogenic, and the skotochromogenic types.[29]

Our interest in the atypical acid-fast infections stems from the fact that, in the district served by our hospital, 35 per cent of patients with positive sputum cultures yield atypical acid-fast bacilli in their cultures. Of these atypical cultures, 18.4 per cent are of the photochromogenic group and 67.8 per cent are classified as skotochromogenic.

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In our early experience, the atypical infections were regarded not unlike typical acid-fast infections with regard to chemotherapy schedules and surgical therapy. However, in managing cases of photochromogenic acid-fast infection, it soon became apparent that we were confronted with an organism resistant to conventional chemotherapy and a disease process that produces a higher surgical complication rate following limited type resections than was experienced in the treatment of typical acid-fast infections. Because of the large concentration of this type of case in our area and, consequently, a wider surgical experience in this type of infection than has been reported elsewhere to date, it was thought that an analysis of these cases would be profitable.

The following report will attempt to define the presently recognized types of atypical infections encountered, the clinical characteristics of these diseases, the role of chemotherapy and surgery in such infections, and the histopathologic findings in surgical specimens. An attempt will be made to explain the higher incidence of surgical complications encountered in the photochromogenic infections and to present our current views on surgical therapy in such infections.

CLINICAL MATERIAL

Case records of patients treated and undergoing surgery at Suburban Cook County Tuberculosis Hospital Sanitarium between June 1, 1955, and Jan. 1, 1959, and later followed as outpatients, form the basis of this report.

METHODS

Bacteriology.—Selected material from sputum and from resected lung tissue was studied by direct smear, culture on Lowenstein-Jensen medium, evaluation of drug resistance (streptomycin, isoniazid, and para-aminosalicylic acid), and guinea pig inoculation. Judging a positive culture to be atypical was based on the (1) careful examination of properly stained smears, (2) the systematic observation of colonial morphology, (3) the development of or change in colony pigmentation after exposure to light during the active phase of growth, and (4) the results observed after intraperitoneal and subcutaneous inoculations into guinea pigs. Details of methods employed have been described earlier.[27] On this basis, atypical organisms can be classified into four groups as follows.

I. *Photochromogenic acid-fast bacilli:* The principal distinguishing feature of these strains is that the colonies are capable of acquiring a golden or lemon-yellow color after exposure to light. The colonies usually are quite smooth. In general, the photochromogenic strains produce a recognizable growth in 10 to 14 days on primary isolation. Guinea pig inoculation with the photochromogenic strains demonstrates that these organisms are much less virulent than typical tubercle bacilli. Subcutaneous injection of the photochromogenic strains in the guinea pig gives rise to local abscesses at the site of injection with little evidence of further spread of disease Intraperitoneal injection of these organisms produces an infection involving the serous surfaces of the omentum, liver, and spleen, giving rise to superficial, caseous nodules containing the atypical acid fast bacilli Both intraperitoneal and subcutaneous inoculations of these organisms produce tuberculin sensitivity in guinea pigs[21]

II *Skotochromogenic acid fast bacilli:* This group of atypical acid-fast organisms produces orange to brick-red pigmented colonies when grown in the dark There is a wide range of colony morphology from large and flat to small and dome shaped The skotochromogenic strains usually require 3 to 4 weeks incubation to become apparent at the time of primary isolation Guinea pig inoculation, either intraperitoneal or subcutaneous, with these organisms fails to demonstrate significant virulence although the majority of injected animals become tuberculin positive However, no progressive or invasive disease occurs and the animals rarely die

III *Nonphotochromogenic strains (Battey type):* These organisms produce colonies which are variable in pigmentation ranging in color from buff to light orange but are not altered by exposure to light The colonies are smooth, moist, and often appear as a confluent, buff colored film with an occasional large colony rising out of the diffuse growth The cells are shorter and more coccoid than are typical tubercle bacilli The inoculation of many of these strains into guinea pigs results in progressive disease grossly indistinguishable from that produced by typical human type cultures

IV *Rapidly growing atypical strains* These strains are recognized and categorized on the basis of their ability to grow rapidly on artificial media to the extent that adequate colonial growth is visible by the seventh day of incubation The colonies are cream to buff in color and do not develop any additional pigmentation after exposure to light These cultures fail to produce invasive or progressive disease in guinea pigs These organisms are distinguished primarily by their complete resistance in vitro to streptomycin, PAS, and isoniazid

Pathology—Surgical specimens from patients undergoing pulmonary resection were submitted to the pathologist for gross and histopathologic study Employing sterile technique, material was removed from each specimen for study, which included microscopic examination, culture, and animal inoculation

OBSERVATIONS

Surgical experience in the atypical infections has been primarily limited to the photochromogenic and skotochromogenic types and therefore each of these groups will be considered separately

Photochromogenic Infections—One hundred and eight patients with pulmonary disease caused by atypical photochromogenic acid fast bacilli have been reported from our laboratory, representing 7 8 per cent of all positive cultures and 18.4 per cent of all atypical cultures. Twenty-four of these patients have undergone 30 surgical procedures in the course of their treatment. Clinical data on these patients are tabulated in Table I.

The average age of these patients was 41 years and they ranged in age from 24 to 63 years. Eighteen (75 per cent) of these patients were males and 6 (25 per cent) were females.

Seven of these patients entered the hospital with the roentgenographic classification of "far advanced" and 17 were classed as "moderately advanced." Four of the patients demonstrated bilateral disease, and cavitary disease was present in all cases. The most striking roentgenographic finding in these cases was the presence of thin-walled cavities—this observation being made in nearly one half of the cases (Figs. 1-3). These cavities ranged in size from 1 to 5 cm. in diameter and not infrequently were solitary isolated cavities. Otherwise, the x-ray appearance of this disease was similar to and indistinguishable from typical pulmonary tuberculosis.

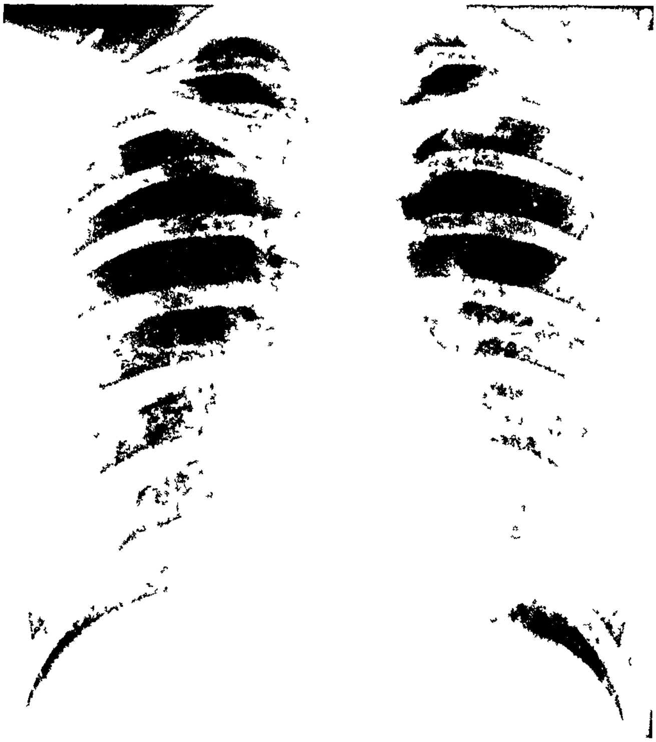

Fig. 1.—C. C., 26-year-old woman. Admission roentgenogram revealed a 1.5 cm. thin-walled cavity in left subapical area. Sputum was smear and culture positive for atypical photochromogenic acid-fast bacilli.

All but one of these patients yielded positive sputum cultures for photochromogenic mycobacteria on admission. The cultures were studied in terms of their resistance to streptomycin, isoniazid, and PAS. All of the cultures were obtained prior to the initiation of antituberculous chemotherapy and thereby characterize the original pretreatment levels of drug resistance encountered in these photochromogenic acid-fast cultures. These atypical cultures uniformly manifested significantly elevated resistance to all of the

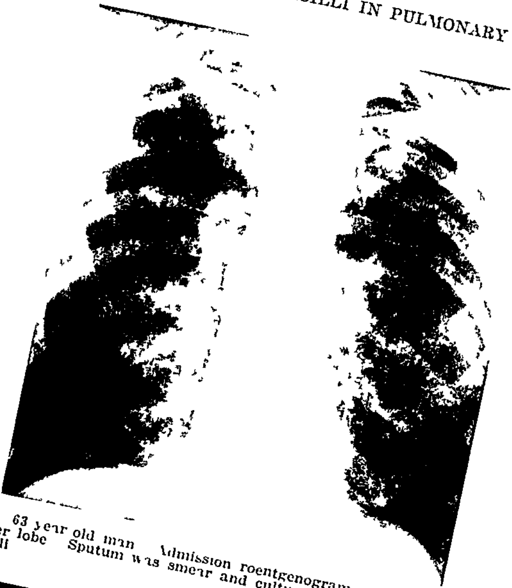

Fig 2—I N 63 year old man Admission roentgenogram revealed a 5 cm thin wa
cavity in right upper lobe Sputum was smear and culture positive for atypical photochrom
genic acid fast bacilli

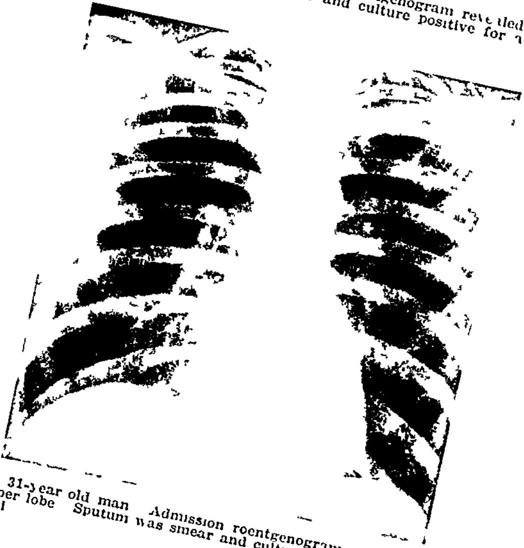

Fig 3—T H 31-year old man Admission roentgenogram revealed a 3 cm thin walled cavity in the left upper lobe Sputum was smear and culture positive for atypical photochromogenic acid fast bacilli

Table I. Clinical Data and Surgica ence in 24 Patients With Atypical Photochromogenic Acid-Fast Infections

PATIENT	AGE SEX	ROENTGENOGRAPHIC CLASSIFICATION ON ADMISSION TO HOSPITAL	CHEMOTHERAPY*	MONTHS OF CHEMOTHERAPY PRIOR TO SURGERY	ROENTGENOGRAPHIC RESPONSE TO THERAPY PRIOR TO SURGERY	PRESURGICAL BRONCHOSCOPIC FINDINGS	SPUTUM CULTURE STATUS AT SURGERY	TYPE OF SURGERY†	MAJOR COMPLICATIONS	ULTIMATE END RESULTS
L. B.	62M	Far advanced; thin-walled cavity in right apex; thick-walled cavity in left upper lobe	INH PAS SM	7	Persistent bilateral upper lobe cavities	Grade II endobronchitis	Negative	Left plombage thoracoplasty	None	Good
R. C.	51M	Moderately advanced; left apical cavity; nodular densities in right upper lobe	INH PAS SM	4	Persistent left upper lobe cavity	Grade II endobronchitis	Negative	Apical posterior segmental resection of left upper lobe	None	Good
C. Ci.	26F	Moderately advanced; 1.5 cm. thin-walled cavity in left upper lobe	PAS SM	9	Persistent thin-walled cavity in left upper lobe, smaller than on admission	Normal	Negative	Subsegmental resection of left upper lobe	None	Good
C. Cl.	34M	Moderately advanced; fibrocavitary disease in right upper lobe	INH+ PAS SM+	12	Slight clearing; persistent cavity in right upper lobe	Grade I endobronchitis	Positive	Right plombage thoracoplasty	None	Good
G. C.	24F	Moderately advanced; 2.5 cm. isolated thin-walled cavity in left upper lobe	INH PAS SM	3	Closure of cavity	Normal	Negative	Subsegmental resection of left upper lobe	Culture positive 4 months postop.	Good
W. D.	54M	Moderately advanced; right apical infiltrate with 1-2 cm. cavities	INH+ SM	5	Slight clearing; persistent cavitary disease in right apex	Grade I endobronchitis	Positive	Right plombage thoracoplasty	None	Good

							Positive	Right plombage thoracoplasty	None	Good
	46M	Far advanced; bilateral cavitary disease	INH+ PAS SM	5	Clearing of right lung lesion; persistent thin-walled cavity in left apex	Grade I endobronchitis	Negative	Left plombage thoracoplasty	None	Good
S. H.	43M	Far advanced; 5 cm. thick-walled cavity in left upper lobe	INH PAS SM	13 (irregularly)	Clearing of infiltrate; reduction of size of cavity	----	Positive	Apical posterior segmental resection of left upper lobe	Broncho-pleural fistula with empyema	----
		----	INH PAS SM+	14 (irregularly)	Left apical airspace	----	Positive	Left 4 rib thoracoplasty	Persistent broncho-pleural fistula with empyema; persistently positive sputum	----
		----	INH+ PAS SM	21 (irregularly)	Persistent left apical empyema; cavity in superior segment of left lower lobe	Traction deformity of left upper lobe bronchus; no endobronchitis	Positive	Left pleural pneumonectomy	None	Good
T. H.	31M	Moderately advanced; 3 cm. isolated thin-walled cavity in left upper lobe	INH SM	7	Clearing of infiltrate; persistent small cavity in left upper lobe	Normal	Negative	Apical posterior segmental resection of left upper lobe	None	Good
E. K.	48M	Far advanced; cavitary disease in left upper lobe	INH PAS SM	7	Minimal clearing; persistent thin-walled cavities in le	Normal	Positive	Left		

TABLE I. CLINICAL DATA AND SURGICA IENCE IN 24 PATIENTS WITH ATYPICAL PHOTOCHROMOGENIC ACID-FAST INFECTIONS

PATIENT	AGE SEX	ROENTGENOGRAPHIC CLASSIFICATION ON ADMISSION TO HOSPITAL	CHEMOTHERAPY*	MONTHS OF CHEMOTHERAPY PRIOR TO SURGERY	ROENTGENOGRAPHIC RESPONSE TO THERAPY PRIOR TO SURGERY	PRESURGICAL BRONCHOSCOPIC FINDINGS	SPUTUM CULTURE STATUS AT SURGERY	TYPE OF SURGERY†	MAJOR COMPLICATIONS	ULTIMATE END RESULTS
L. B.	62M	Far advanced; thin-walled cavity in right apex; thick-walled cavity in left upper lobe	INH PAS SM	7	Persistent bilateral upper lobe cavities	Grade II endobronchitis	Negative	Left plombage thoracoplasty	None	Good
R. C.	51M	Moderately advanced; left apical cavity; nodular densities in right upper lobe	INH PAS SM	4	Persistent left upper lobe cavity	Grade II endobronchitis	Negative	Apical posterior segmental resection of left upper lobe	None	Good
C. Ci.	26F	Moderately advanced; 1.5 cm. thin-walled cavity in left upper lobe	PAS SM	9	Persistent thin-walled cavity in left upper lobe, smaller than on admission	Normal	Negative	Subsegmental resection of left upper lobe	None	Good
C. Cl.	34M	Moderately advanced; fibrocavitary disease in right upper lobe	INH+ PAS SM+	12	Slight clearing; persistent cavity in right upper lobe	Grade I endobronchitis	Positive	Right plombage thoracoplasty	None	Good
G. C.	24F	Moderately advanced; 2.5 cm. isolated thin-walled cavity in left upper lobe	INH PAS SM	3	Closure of cavity	Normal	Negative	Subsegmental resection of left upper lobe	Culture positive 4 months	Good
.D.	54M	Moderately advanced; right apical infiltrate with 1-2	INH+ SM	5	Slight clearing;					

		…ar advanced; bilateral cavitary disease	INH PAS SM	5	Clearing of right lung	…ormal	Positive	Right plombage thoracoplasty	None	Good
S. H.	13M	Far advanced, 5 cm thick walled cavity in left upper lobe	INH PAS SM	11 (irregularly)	…sistent thin walled cavity in left apex	Grade 1 endobronchitis	Negative	Left plombage thoracoplasty	None	Good
					Clearing of infiltrat… …of cavity		/	Apical posterior segmental resection of left upper lobe	Bronchopleural fistula with empyema	----
			INH PAS SM	11 (irregularly)	Left apical airspace	----	Positive	Left 4 rib thoracoplasty	Persistent bronchopleural fistula with empyema; persistently positive sputum	----
			INH PAS SM	21 (irregularly)	Persistent left apical empyema; cavity in superior segment of left lower lobe	Traction deformity of left upper lobe bronchus; no endobronchitis	Positive	Left pleural pneumonectomy	None	Good
F. H.	31M	Moderately advanced; 3 cm. isolated thin-walled cavity in left upper lobe	INH SM	7	Clearing of infiltrate; persistent small cavity in left upper lobe	Normal	Negative	Apical posterior segmental resection of left upper lobe	None	Good
K.	48M	Far advanced; cavitary disease in left upper lobe	INH PAS SM	7	Minimal clearing; persistent thin-walled cavities in left u…	Normal	Positive	Left pl…		
			INH							

TABLE I—(CONT'D)

PATIENT	AGE SEX	ROENTGENOGRAPHIC CLASSIFICATION ON ADMISSION TO HOSPITAL	CHEMOTHERAPY*	MONTHS OF CHEMOTHERAPY PRIOR TO SURGERY	ROENTGENOGRAPHIC RESPONSE TO THERAPY PRIOR TO SURGERY	PRESURGICAL BRONCHOSCOPIC FINDINGS	SPUTUM CULTURE STATUS AT SURGERY	TYPE OF SURGERY†	MAJOR COMPLICATIONS	ULTIMATE END RESULTS
J. M.	57M	Moderately advanced; fibrocavitary disease in right upper lobe	INH+ PAS SM	5	No response	Grade II endobronchitis	Negative	Right plombage thoracoplasty	Persistently positive sputum	Poor
E. M.	40F	Moderately advanced; multiloculated cavity in right upper lobe	INH SM	5	No response	Normal	Positive	Apical posterior segmental resection of right upper lobe	Bronchopleural fistula with empyema	----
		----	INH SM	11	Persistent right apical empyema	----	Negative	Right plombage thoracoplasty	None	Good
J. N.	60M	Far advanced; 1-2 cm. thick-walled cavities in right upper lobe	INH+ SM	15	Clearing of infiltrate; persistent cavities in right upper lobe	Grade I endobronchitis	Positive	Right plombage thoracoplasty	Persistently positive sputum	Fair
E. N.	63M	Far advanced; 5 cm. thin-walled cavity in right upper lobe	INH PAS SM	7	Moderate clearing of infiltrate; reduction of size of cavity	Normal	Negative	Right plombage thoracoplasty	None	Good
F. O.	37M	Moderately advanced; small cavity in right upper lobe with pericavitary infiltrate	INH+ PAS SM+	4	Persistent cavity with clearing of infiltrate	Normal	Negative	Right plombage thoracoplasty	None	Good
R. P.	40M	Moderately advanced; cavitary dis-	INH+ SM+	4	No response	Normal	Negative	Right plombage thoracoplasty	None	Good

		…ed cavity in right apex	PAS SM		No response	Normal	Negative	Subsegmental resection of right upper lobe	None	Good
H S	31M	Moderately advanced, 3 cm isolated thin walled cavity in right upper lobe	INH SM+	2	No response	Grade I endobronchitis	Negative	Apical posterior segmental resection of right upper lobe	None	Good
G S	26F	Moderately advanced, soft infiltrate in left upper lobe with small cavity	INH PAS SM+	4	Moderate clearing with cavity closure	Normal	Negative	Subsegmental resection of left upper lobe	None	Good
E S	43M	Moderately advanced, bilateral disease with right upper lobe cavity	INH PAS SM	4	Clearing of infiltrates; residual cavity in right upper lobe	Normal	Positive	Right plombage thoracoplasty	None	Good
F T	50M	Far advanced; large cavity in left upper lobe	INH SM	4	Minimal clearing, persistent large apical cavity	Normal	Negative	Left plombage thoracoplasty	None	Good
C U	43M	Moderately advanced, thick-walled cavity in right apex	INH PAS SM+	5	No response	Grade I endobronchitis	Negative	Apical posterior segmental resection of right upper lobe	Bronchopleural fistula with empyema	----
		----	INH PAS SM+	6	Right apical empyema	----	Negative	Right plombage thoracoplasty	None	Good
W. W.	30M	Moderately advanced, 3 4 cm cavities in left upper lobe	INH+ PAS SM+	6	Clearing of infiltrate; residual small cavities in left upper lobe	Normal	Negative	Left upper lobectomy	None	

*INH = Isoniazid 300 mg daily
INH+ = Isoniazid 600-1 200 mg daily
PAS = para-aminosalicylic acid
SM = streptomycin
SM+ = st

standard antituberculous drugs but most strikingly with regard to streptomycin and PAS. This finding is, in our experience, typical of photochromogenic cultures. The average duration of chemotherapy in these patients prior to surgery was 6 months, ranging from 2 to 15 months as tabulated in Table I. Early dosage schedules in these cases were "conventional," i.e., isoniazid 300 mg. daily, PAS 12 Gm. daily, and streptomycin 1 Gm. twice weekly. More recently, larger dosages of isoniazid and streptomycin have been employed in some cases, isoniazid 600 to 1,200 mg. daily and streptomycin 1 Gm. daily. In general, the roentgenographic response to therapy was unimpressive. Slight to moderate clearing of infiltrates was observed in 14 cases. In 6 cases, the cavity reduced in size and in 3 instances cavity closure was noted. Six patients showed essentially no roentgenographic response to therapy prior to surgery.

Surgical experiences in the photochromogenic infections are tabulated in Table I and summarized in Table II.

TABLE II. EXPERIENCE IN THE SURGICAL TREATMENT OF 24 PATIENTS WITH ATYPICAL PHOTOCHROMOGENIC ACID-FAST INFECTIONS

TYPE OF SURGERY	NUMBER OF CASES	MAJOR COMPLICATIONS	COMPLICATION RATE
Subsegmental resection	5	2 reactivation or recurrence of disease	40 %
Segmental resection	6	3 bronchopleural fistulas with empyema	50 %
Lobectomy	1	0	0
Pneumonectomy	2	0	0
Plombage thoracoplasty	15	3 failure to convert sputum	20 %
Conventional thoracoplasty	1	1 failure to close bronchopleural fistula and convert sputum	100 %

Fourteen pulmonary resections were performed for photochromogenic acid-fast infections. Five of these were of the subsegmental or wedge type, six segmental resections, one lobectomy, and two pneumonectomies.

Two of the 5 patients undergoing subsegmental resections developed major postoperative complications in the form of recurrence or reactivation of disease. Positive sputum cultures were obtained 5 and 15 months postoperatively. One of these patients subsequently underwent a paraffin plombage thoracoplasty that resulted in sputum conversion. The remaining 3 patients with subsegmental resections did not experience any major postoperative complications. This would represent a complication rate of 40 per cent for subsegmental resection.

Three of the 6 patients treated by segmental resection developed bronchopleural fistulas with empyema postoperatively. These fistulas and empyema spaces were treated by surgical collapse procedures—conventional thoracoplasty in one instance and paraffin plombage thoracoplasty in 2 cases. The two plombage thoracoplasties resulted in control of the fistulas and obliteration of the empyema spaces, but the conventional thoracoplasty failed to control the fistula and empyema space. Subsequently, in the latter case, because of persistently positive sputum cultures, it was necessary to perform a pleural pneumonectomy for control of the patient's disease These 3 cases out of the total of 6 segmental resections would represent a complication rate of 50 per cent

The single patient treated by lobectomy for photochromogenic infection experienced no postoperative complications

The two pneumonectomies performed in the photochromogenic group represent secondary procedures after other surgical procedures had failed to control the disease One case has been described above under the segmental resection group The other case represents a failure of paraffin plombage thoracoplasty to close the cavitary disease and achieve sputum conversion, thereby leading to pneumonectomy for control of the disease Postoperatively major complications were not encountered in either case

Sixteen surgical collapse procedures were carried out in an attempt to control atypical photochromogenic infections (Table I), 15 of these were of the paraffin plombage thoracoplasty type while a conventional type thoracoplasty was employed in 1 case Failure of the thoracoplasty to collapse cavitary disease and result in sputum culture conversion or to obliterate a postresection empyema space and result in closure of a bronchopleural fistula was observed in 4 cases representing 25 per cent of all cases in which collapse therapy was performed

In spite of this high postsurgical complication rate, 91 5 per cent of all the patients with photochromogenic acid fast infections treated by surgery ultimately experienced a good result with respect to adequate control of their pulmonary disease

The tissues from the photochromogenic cases demonstrated the whole gamut of the anatomic and histopathologic findings seen in typical human type *Mycobacterium tuberculosis,* var *hominis* No organisms other than acid fast bacilli were encountered in the lesions The cases with photochromogenic infection, however, exhibited distinct histopathologic differences Nearly all of the surgical specimens contained cavities communicating widely with bronchi The cavity walls and adjoining lung parenchyma exhibited an abundance of granulomatous tissue and tubercles containing giant cells, epithelioid cells, and caseation necrosis The cavities were irregular in shape and lined by active granulation tissue While most portions of their walls were thin and devoid of a distinct limiting fibrous periphery, in some portions they were encroached upon by irregular confluent solid foci containing an admixture of caseous material, zones of dense fibrous tissue, and granulation tissue in various stages of organization These foci were ill defined, moderately firm, often yellow, and devoid of a capsule They were often in close proximity to bronchi The solid foci were set close together and there was little bronchogenic dissemination The most outstanding pathologic feature in over 90 per cent of cases was involvement of the bronchi by the disease process The lesions were not merely restricted to the bronchus draining a specific focus but extended toward the hilum of the lobe via the submucosal lymphatics and

TABLE III. CLINICAL DATA AND SURGICAL EXPERIENCE IN 10 PATIENTS WITH ATYPICAL SKOTOCHROMOGENIC ACID-FAST INFECTIONS

PATIENT	AGE SEX	ROENTGENOGRAPHIC CLASSIFICATION ON ADMISSION TO HOSPITAL	CHEMOTHERAPY*	MONTHS OF CHEMOTHERAPY PRIOR TO SURGERY	ROENTGENOGRAPHIC RESPONSE TO THERAPY PRIOR TO SURGERY	PRESURGICAL BRONCHOSCOPIC FINDINGS	SPUTUM CULTURE STATUS AT SURGERY	TYPE OF SURGERY	MAJOR COMPLICATIONS	ULTIMATE END RESULTS
K. B.	41M	Minimal; small circumscribed density in right upper lobe	INH PAS SM	1½	No response	Normal	Negative	Subsegmental resection of right upper lobe	None	*Good*
A. C.	37F	Moderately advanced; fibronodular disease in left upper lobe	INH PAS SM	12	Minimal clearing	Normal	Negative	Left upper lobectomy	None	Good
J. G.	26M	Minimal; infiltrate in left upper lobe	INH+ PAS SM	3	Small cavities in left upper lobe	Normal	Negative	Apical posterior segmental resection of left upper lobe	None	Good
H. G.	56M	Far advanced; bilateral fibrocavitary disease	INH PAS SM	30	Persistent cavity in left upper lobe; bronchiectasis in right upper lobe	Normal	Negative	Left plombage thoracoplasty	Sputum culture positive for 6 months then converted	Good
W. H.	29M	Minimal; small circumscribed density in right upper lobe	INH+ PAS SM+	3	No response	Normal	Negative	Subsegmental resection of right upper lobe	None	Good

R M	33F	Moderately advanced, large cavity in right upper lobe	INH PAS SM	6	Persistent cavity in right upper lobe	Normal	Negative	Right plombage thoracoplasty	None	Good
E Mc.	40F	Minimal, infiltrate in right infraclavicular region	INH+ SM	4	Small cavity in right infraclavicular region	Normal	Negative	Apical posterior segmental resection of right upper lobe	None	Good
C N.	51M	Moderately advanced, fibrocavitary disease in right apex	INH SM	4	No response	Grade I endobronchitis	Negative	Right plombage thoracoplasty	Persistently positive sputum 2 months postop.	Lost to follow-up
G. O.	20F	Minimal; infiltrate in right apex	INH PAS SM+	7	No response	----	Negative	Subsegmental resection of right upper lobe	None	Good
H Q.	63M	Moderately advanced, fibrocavitary disease in right upper lobe; minimal infiltrate in left upper lobe	INH+ PAS SM	3	No response	Normal	Negative	Right plombage thoracoplasty	None	Good

*See Table I for key to symbols

ranged from frank ulceration to mild subepithelial lesions. The incidence of this pathologic pattern was much higher than that observed in a comparable group of cases with typical tuberculosis (29 per cent). The amount of both free and phagocytosed fat, including birefringent material, was also greater in the cases of photochromogenic infections. Large numbers of histiocytes and giant cells contained small fat droplets, and numerous lipoid inclusions were noted within giant cells. Asteroid bodies were encountered in 40 per cent of cases and Schaumann bodies in 30 per cent.

Skotochromogenic Infections.—Ten patients yielded cultures positive for skotochromogenic acid-fast bacilli prior to undergoing surgical therapy. Clinical data on these patients are tabulated in Table III. The average age of these patients was 40 years, ranging from 20 to 63 years. Six of the patients were males and 4 were females. One of these patients entered the hospital with roentgenologic findings of far-advanced disease. Four of the cases were classified as moderately advanced and 5 as minimal. Five of these patients, on admission to the hospital, yielded sputum cultures positive for typical acid-fast bacilli and in the course of their treatment converted to yielding atypical skotochromogenic acid-fast bacilli on culture. Five of these patients were admitted to the hospital with sputum cultures initially positive for skotochromogenic organisms.

Drug resistance studies on the skotochromogenic cultures revealed moderately elevated resistances to streptomycin, PAS, and isoniazid. These increased resistances are observed even when these strains are isolated from patients who have received no prior chemotherapy. The average duration of chemotherapy in these patients prior to surgery was 7 months, ranging from 1½ to 30 months. Dosage schedules, in general, were isoniazid 300 mg. daily, PAS 12 Gm. daily, and streptomycin 1 Gm. twice weekly.

In general, little response to therapy was observed by x-ray examination in the skotochromogenic infections. Five cases showed essentially no change during the course of therapy prior to undergoing surgery. Two infiltrative lesions were observed to cavitate during therapy while in 3 other cases cavitary disease was only minimally altered during the presurgical therapy period.

Surgical experiences in the skotochromogenic infections are tabulated in Table III. Six pulmonary resections were performed for the skotochromogenic infections—three subsegmental resections, two segmental resections, and one lobectomy. No major postoperative complications were encountered in this group of resections. Four paraffin plombage thoracoplasties were performed in patients with skotochromogenic infections. The results of this surgical collapse therapy in these infections compares favorably with our observations in typical acid-fast infections.

Histopathologic examination of surgical specimens obtained from patients with skotochromogenic infections revealed findings not dissimilar to typical tuberculosis. No distinguishing characteristics or differences were attributable to these infections.

Typical Acid-Fast Infections.—Table IV summarizes the surgical results in 153 cases of typical acid-fast infections treated during the period of time covered by our observations on the atypical infections and is included for comparison to the results in the atypical groups.

TABLE IV. EXPERIENCE IN THE SURGICAL TREATMENT OF 153 PATIENTS WITH TYPICAL ACID-FAST INFECTIONS

TYPE OF SURGERY	NUMBER OF CASES	MAJOR COMPLICATIONS	COMPLICATION RATE
Subsegmental resection	14	0	0
Segmental resection	28	2 bronchopleural fistulas and/or empyema 2 persistently positive sputum postop. 2 reactivation or recurrence of disease	21.4 %
Lobectomy	34	4 bronchopleural fistulas and/or empyema 1 persistently positive sputum postop. 1 reactivation or recurrence of disease	17.6 %
Pneumonectomy	11	1 bronchopleural fistula with empyema 1 contralateral spread of disease 2 deaths	36.4 %
Plombage thoracoplasty	62	16 failure to convert sputum 1 spread of disease	27.4 %
Conventional thoracoplasty	4	1 failure to convert sputum	25 %

DISCUSSION

Photochromogenic Acid-Fast Infections.—Photochromogenic acid-fast organisms, also known as the "yellow" acid-fast bacillus, are invariably isolated from patients with demonstrable pulmonary disease.[21] Usually no other type or strain of acid-fast organism is ever recovered from these patients and in their surgical or autopsy specimens only photochromogenic organisms have been recovered.

When adding the morphologic and bacteriologic evidence together with the clinical picture, there seems little reason to doubt that these atypical mycobacteria are etiologically related to the pulmonary disease seen in the patients producing sputum positive for these organisms. It is not clear at this time whether these organisms should be viewed as variants of human-type tubercle bacilli or whether they represent infections with some other species of mycobacteria. Eighty-five per cent of all photochromogenic infections studied occurred in males and only 15 per cent of such cases were found in females. The preponderance of male cases of photochromogenic infection would suggest that the transmission of this type of disease is less likely to be primarily on a familial or household basis. None of the patients with photochromogenic infections demonstrated significant exudative or inflam components in their disease during our observation. The cases extent from minimal to far advanced but all seemed to be characterized by their chronic fibrocavitary quality and were especially prone to develop indolent thin-walled cavities. No instances of hematogenous or acute intrapulmonary dissemination were encountered nor were any renal, bone and joint, or other extrapulmonary lesions found.

The photochromogenic cultures uniformly manifest significantly elevated resistance to all of the standard antituberculous drugs, but this is most strikingly seen with regard to streptomycin and PAS. Patients with this type infection respond poorly to conventional chemotherapy schedules. It seems probable that much if not all of the failure to respond to chemotherapy might be explained on the basis of the pretreatment resistance of these photochromogenic strains to the antituberculous drugs. However, there may be other still unknown factors related to the basic biologic characteristics of these organisms which may determine their failure to respond to chemotherapy.

Comparison of the lesions due to photochromogenic infections with typical tuberculous disease reveals differences in (1) composition of the tuberculous foci, (2) extent of endobronchial disease, and (3) amount and character of ingested and free fat. In the photochromogenic cases, the lesion commonly consists of irregular conglomerate solid foci bordering an otherwise thin-walled cavity. Although much connective tissue is discernible around some parts of the cavity wall, and within several portions of the conglomerate foci, the peripheral portions of the cavities and of the individual solid foci are generally ill defined and lack fibrous encapsulation. The process appears to grow by contiguity and direct extension rather than bronchogenic dissemination. The intimate admixture of advanced organization with active granulomatous disease and the poor encapsulation suggest an active, though slowly progressive, process, such as may be caused by resistant organisms of low virulence. The low virulence of the organisms may also account for the relative lack of bronchogenic dissemination in the presence of severe endobronchial disease. The excessive amounts of fat and Schaumann bodies noted, likewise, may be the result of the biologic characteristics of the photochromogenic organisms. In analyzing the surgical complication rate in the group of photochromogenic infections, it is recognized that small numbers of cases are involved in each series and therefore percentages are less meaningful. Nevertheless, the complication rates observed are of such a magnitude that they undoubtedly have real significance. It has been observed that in the cases of photochromogenic infections in which resection was performed and complications followed, all were limited type resections—subsegmental or segmental. Furthermore, 3 of the 5 patients had positive sputum cultures at the time of surgery and mild endobronchitis was present in 1 case, as observed on bronchoscopic examination. It is felt that the increased drug resistance of these organisms and even more importantly, the basic disease process, i.e., the high incidence of endobronchial disease and the poorly demarcated cavitary and solid foci, are important factors in explaining the high rate of postoperative complications observed in our series. Therefore, greater attention should be paid to achieving negative sputum culture status and bronchoscopic evidence of absence of endobronchial involvement prior to undertaking surgical therapy. Surgical resection should then be employed in such a manner as to circumscribe more widely the disease process than in the treatment of typical acid-fast infections. In most cases this would indicate lobectomy as the minimal type of resection to be employed.

Skotochromogenic Acid-Fast Infections.—The skotochromogenic strains undoubtedly represent a much less homogeneous group of acid fast organisms than do the photochromogenic mycobacteria. In general, the skotochromogenic strains frequently resemble many of the well characterized saprophytic species of mycobacteria and on occasion they demonstrate attributes of Nocardia and other fungi. These organisms have been referred to by other writers as "chromogenic" acid fast bacilli or the "orange" bacilli.[5, 10, 18, 22]

The majority of isolations of these organisms have come from patients demonstrating chronic pulmonary disease who have been positive for typical tubercle bacilli at some time prior to the isolation of the atypical, pigmented cultures. These patients never showed further progression of their pulmonary disease during the period when the skotochromogenic organisms were isolated. On the other hand we have consistently failed to isolate skotochromogenic acid fast bacilli from patients with no detectable pulmonary disease. The absence of significant resistance to any single antituberculous drug on the part of skotochromogenic cultures makes it difficult to believe they can be accounted for on the basis of drug resistant mutants or variants. However this possibility cannot be eliminated entirely.

These organisms appear to have definite significance in terms of the biologic history of tuberculosis in the individuals from whom they are isolated. In general, we feel that the presence of such atypical cultures is a good prognostic omen. However, inasmuch as the majority of these patients were culture positive for typical organisms in their immediate past, we feel that full and adequate chemotherapy should be continued until the traditional criteria for cessation of treatment are fulfilled plus complete absence of the bacilli on repeated culture. Recovery of skotochromogenic strains was rarely followed at a later time by the isolation of typical cultures from the same patient.

Our limited surgical experience in the group of patients yielding the skotochromogenic type of organism would bear out the reduced pathogenicity of these organisms. The incidence of major complications following surgery in this group was found to compare favorably with our experience in the management of typical acid fast infections. Consequently, it is not felt that these atypical skotochromogenic acid fast organisms present any unusual problems in surgical management.

SUMMARY AND CONCLUSION

1. Thirty-five per cent of patients with positive sputum cultures in the district served by our hospital yield atypical acid-fast bacilli.
2. A brief description of the four types of atypical acid-fast bacilli found on culture is presented.
3. Of the atypical cultures, 18.4 per cent are of the photochromogenic group and 67.8 per cent are skotochromogenic.
4. Surgical experiences in the two major groups of atypical infections are presented and compared with the surgical results in typical infections during the same period of time.
5. The postoperative complication rate in the limited resection cases (subsegmental and segmental resections) of photochromogenic infection was found to be strikingly greater than in the skotochromogenic or typical acid-fast infections.
6. Histopathologic comparison of the lesions due to photochromogenic infections with typical tuberculous disease reveals differences in composition of the tuberculous foci, extent of endobronchial disease, and amount and character of ingested and free fat.
7. It is believed that the high rate of postoperative complications observed in our series of photochromogenic infections can be largely explained on the basis of these pathologic processes and the increased drug resistance of these organisms.
8. On the basis of these observations, it is our opinion that photochromogenic acid-fast infections should be regarded with a much more conservative and cautious attitude regarding surgical resection therapy, and that the application of resections of less than lobar extent are hazardous.

We wish to acknowledge the technical assistance of Miss Rosemary Colton.

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DISCUSSION

DR ROBERT T FOX, Glenview, Ill—I want to congratulate Dr Harrison on this beautiful piece of work and its presentation I trust this isn't strictly a Chicago and vicinity problem I am sure others have had the same trouble But knowing of their trouble with this, we at Chicago Municipal Tuberculosis Sanitarium reviewed some of our figures and, in just the year of 1957, found that of roughly 200 patients with pulmonary resection, other than pneumonectomies, about 25, or one eighth, had somewhere or another in their course photochromogenic organisms cultured. Of that 25, the incidence of complications of various types ran about 40 per cent, similar to Dr. Harrison's, whereas in the complications of cases with ordinary or typical acid-fast bacilli it ran about 6 or 7 per cent. So there is a very definite factor here.

We have learned to respect this organism and tend, as again Dr. Harrison pointed out, to hit these patients preoperatively if we know that they have these atypical organisms with at least one, preferably two, different antituberculosis drugs, other than those with which they have been managed in their earlier course. During the operation we tend to perform a lobectomy rather than some lesser portion of the lobe, hoping that our incidence of complications will be lower.

We feel that Dr. Harrison's figures certainly compare with ours, and we can't emphasize enough the respect one must give to this atypical bacillus.

If there is any other suspicion of possible impending complication, in addition to the presence of these photochromagens, we tend to do some type of primary collapse procedure rather than resection, hoping we will achieve control of the disease, rather than take the risk of a high incidence of complication.

DR. FRANCIS J. PHILLIPS, Anchorage, Alaska.—I have appreciated hearing this discussion a great deal because it explains a great deal of the problems I have encountered in Alaska in our work there before the sanatorium closed, and my experiences there, on a fewer number of cases, exactly parallel the discussers' experiences here: patients having subsegmental resections did poorly and, in most of these instances, we found this a typical photochromogenic type of growth. We were not able to explain it at that time.

So that it seems to me that in this period of time, when we are sort of forgetting that tuberculosis is a serious problem, we perhaps have to tighten our girdle a little bit and study the cases a little more thoroughly, doing a little more exacting concentration on the type of treatment that we give. It almost, as has been said, carries us to the type of thinking that we had to employ before we had the miracle drugs.

DR. ADAMS (Closing).—In view of our experience with this problem, as Dr. Harrison has told you, and in view of the advent of antimicrobial therapy reducing our surgical problem in tuberculosis, there has been a tendency to do less and less resection in order to preserve as much lung tissue as possible. This brings out the importance of knowing, in this group of cases, just what one is dealing with before surgery.

We see here on a slide the gross characteristics of colonies of both the typical organism in the left upper corner and the *skotochromogenic* (those that become bright orange in the dark) and the *photochromogenic* (which become yellowish orange when exposed to light) types.

If these culture plates are looked at and look suspicious of the photochromogenic type as seen on the left, then microscopic examination will bring out definite evidence of this type of organism.

Therefore, in view of the fact that we are inclined to try to get by with segmental resection or less than segmental, it is well to know the type of organism in advance. I believe by so doing we will lessen still further the magnitude, as well as the percentage, of our complications in these cases.

I wish to thank Dr. Fox and Dr. Phillips for their contributory remarks on this problem.

THE SURGICAL TREATMENT OF TUBERCULOSIS IN CHILDREN

Walter W Fischer, M D, and Peter A del Missier, M D (by invitation), New York, N Y*

PRIOR to the use of specific antibiotics, surgery had very limited application in the treatment of pulmonary tuberculosis in children The prognosis of primary tuberculosis was so grave that few survived for the consideration of surgery Most patients with progressive primary disease died within a year Those who survived were subject to reinfection and spread of the disease Extrapleural procedures commonly performed at that time were not applicable in the treatment of children Thoracoplasty remained the most commonly performed operative procedure in the treatment of adults until streptomycin became available The use of thoracoplasty in children was most often ill advised since it resulted in serious deformity of the growing chest wall and consequent impairment of pulmonary function The advent of antibiotic therapy has radically altered the prognosis of both complicated primary and reinfection tuberculosis in children and has permitted the occasional consideration of surgical treatment Excisional surgery has, in our hands, replaced all less definitive operative procedures Thoracoplasty, extrapleural and extraperiosteal procedures, as well as phrenicotomy, pneumothorax, and pneumoperitoneum, have been completely abandoned

This review is based upon a group of patients treated since 1952 These were patients on the Pediatric Tuberculosis Ward of Bellevue Hospital Center, in addition to the private patients of one of the authors (W W F) Bellevue Hospital serves large segments of the New York metropolitan population in which the incidence of tuberculosis remains high

The patients have been classified in two categories (a) those with adult or reinfection tuberculosis, and (b) those with complicated primary tuberculosis

This classification is used despite the realization that the distinction between primary and secondary tuberculosis is not always clearly defined Primary tuberculosis can occur in adults just as reinfection tuberculosis occurs in children Nevertheless, the entire disease pattern of primary tuberculosis with its characteristic clinical, radiologic, and pathologic findings is usually quite unique The use of this classification is, therefore, considered valid

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Read at the Thirty ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles Calif April 21 23 1959

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Primary tuberculosis heals without incident in the great majority of cases, especially if diagnosed and treated with chemotherapy, when indicated. This discussion concerns the relatively small number of patients who develop complicated primary disease. Complicated primary tuberculosis is subdivided into: (a) progressive primary, and (b) post-primary.

The term progressive primary, as used, defines local progression of the primary parenchymal lesion with or without visible cavitation. Post-primary disease is concerned with the late sequelae of complicated primary tuberculosis. Irreversible pathologic changes, resulting from the lymph node component of the primary complex, are here the outstanding features. Tuberculous infection per se is often completely controlled and secondary infection may then become the principal problem.

Forty surgical cases are reviewed. During the period under consideration, 570 children treated for pulmonary tuberculosis were discharged from the Pediatric Tuberculosis Department of Bellevue Hospital, 300 were male and 270 female. Of these, about 6 per cent had excisional surgery, an approximate ratio of 1 in 17. The age of the patients at the time of surgery varied from 2 to 13 years, the age limit of the Pediatric Service. More specifically, 8 patients were from 2 to 5, 18 from 6 to 10, and 14 from 10 to 13 years of age—16 were male and 24 were female—19 were Puerto Rican, 11 were white, and 10 were Negroes.

Preoperative treatment has varied considerably in the past. Since 1956, a combination of isonicotinic acid hydrazide (INH) and para-aminosalicylic acid (PAS) is used preoperatively, preferably for a period of about 6 months. Streptomycin is usually added at the time of surgery. The postoperative treatment is determined by the proved nature of the disease in the resected specimen as well as the status of the remaining lung observed at operation. Potential surgical cases are discussed in combined pediatric medical-surgical conferences during the course of treatment. Recommended surgical treatment is always a combined decision.

Bronchoscopy is of great value in both diagnosis and treatment of tuberculosis in children. This is particularly true in the primary disease group in which there is a high incidence of tuberculous endobronchitis. Bronchoscopies are performed under general anesthesia to avoid possible trauma, except in infants when anesthesia is not necessary.

Bronchographic examination is performed with increasing regularity. This applies especially to the patients in whom the diagnosis of bronchiectasis seems probable and those with radiologic densities suggestive of persistent atelectasis. Ether anesthesia with endotracheal intubation has superseded the use of rectal anesthetics. Endotracheal intubation affords complete control of the airway as well as a convenient means of introducing contrast material. The latter is thoroughly aspirated after completion of the x-ray examination.

Pulmonary function studies have more recently assumed increasing importance in the preoperative evaluation of patients, particularly those in the post-primary group.

The operative procedures performed are listed in Table I

TABLE I TOTAL NUMBER OF OPERATIONS (40)

TYPE OF OPERATION	TOTAL	R. LUNG	L LUNG	RUL	RML	RLL	RML + RLL	LUL	LLL
Pneumonectomy	6	1	5						
Lobectomy	20	10	10	4	2	1	3	8	2
Segmental resection	14	5	9						

	SEGMENTS							
	APICAL	POST	R SUP	APICAL POST	LINGULA	LINGULA + AMB	APICAL POST + SUP	L SUP
Number of resections	3	1	1	3	2	1	1	2

The postoperative complications were as follows One patient developed empyema necessitating closed drainage 8 days after a left lower lobe lobectomy This same patient eventually died as a result of cardiac arrest which occurred during the excision of a persistent chest wall sinus 3 months after lobectomy This represents the only mortality Two patients developed transitory densities in lobes subjected to segmental resection These cleared with continued chemotherapy There were no bronchopleural fistulas There were no problems related to pulmonary re-expansion following partial resection

In analyzing operative cases, multiple surgical indications are usually present An attempt has been made to identify the single most important factor in each case These dominant indications are listed in Table II Included in this group are 2 indications (No 6 and No 11) considered acceptable but not represented in the operative group

TABLE II INDICATIONS FOR SURGERY

1 Persistent cavitation
2 Noncavitary, bacteriologically positive foci
3 Roentgenologically unstable, probably uncontrolled, caseous lesions
4 "Destroyed" lobe or lung
5 "Tuberculoma" or large, partially calcified foci
6 Acute hilar lymphadenitis
7 Bronchiectasis
   A Symptomatic
   B Asymptomatic but functionally detrimental
8 Persistent atelectasis
9 Bronchostenosis
10 Obstructive emphysema
11 Chronic pleuritis
12 Presence of concomitant disease as complicating factor affecting prognosis adversely
13 The factor of sex and age adversely affecting prognosis

CASE REPORTS

The following are representative cases of the entire group which illustrate the indications listed above

Case 1.—J. V., a 9-year-old Puerto Rican boy, was admitted with a history of chest pain, fever, and productive cough of 4 months' duration. Admission roentgenograms demonstrated infiltration in the lingula. Mantoux was positive (2×). Gastric contents were positive for tubercle bacilli on admission. Specific chemotherapy was instituted with good clinical response. X-ray studies 11 months later suggested some improvement, but tomograms (Fig. 1) revealed persistent cavitation. Lingular segmentectomy was done on Nov. 8, 1952, after 8 months of treatment. The immediate postoperative course was uncomplicated. Caseous, cavitary disease, positive for acid-fast bacilli on direct smear, was present in the surgical specimen. One month after operation, an infiltrate was noticed in the left upper lobe. The previously instituted chemotherapy was supplemented with Aldinamide and was continued for a total of 19 months of treatment with complete clearing.

Comment: X-ray finding of persistent cavitation after 8 months of chemotherapy was the indication for surgery. The lingular location of the lesion was an added indication.

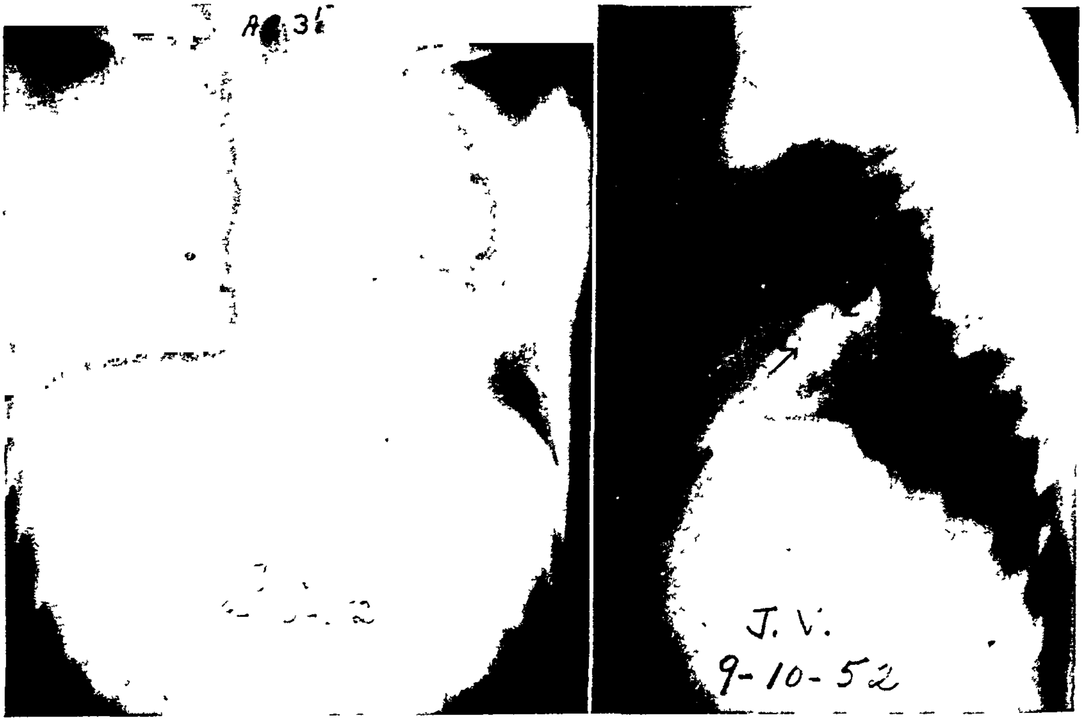

Fig. 1

Case 2.—F. M., a 3-year-old white girl, was admitted with a diagnosis of tonsillitis, pharyngitis, and otitis media. Routine x-ray studies of the chest revealed an area of calcification in the left apex. The patient responded to penicillin and was discharged. One month later, she was readmitted with a diagnosis of bronchitis which was treated with broad spectrum antibiotics. Tomograms (Fig. 2) revealed a large calcified mass. The patient was then transferred to the Chest Service. Patch test for tuberculosis was positive. Gastric washings were positive on 14 consecutive examinations. Bronchogenic spread (Fig. 3), present at the time of admission, cleared after 7 months of specific therapy (Fig. 4). Apical posterior segmental resection was done on Dec. 15, 1955, after 7 months of chemotherapy. The postoperative course was uneventful. Pathologic examination showed a large, dense mass with a caseous center and extensive calcifications at the periphery. Direct smear and culture were positive for acid-fast bacilli. Postoperative gastric content studies were consistently negative. A follow-up x ray study, 2 years after surgery, is presented in Fig. 5.

Comment: This is an example of progressive primary disease with x-ray evidence of marked calcification. The primary indication for surgery was persistent positive sputum in the presence of a densely calcified lesion.

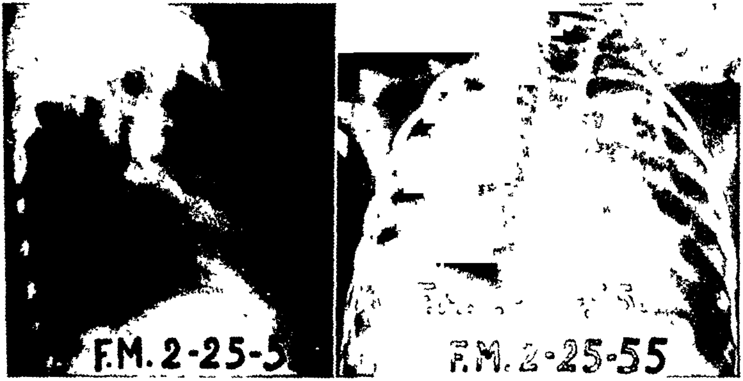

Fig 2

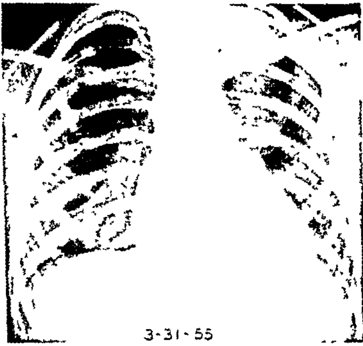

Fig 3

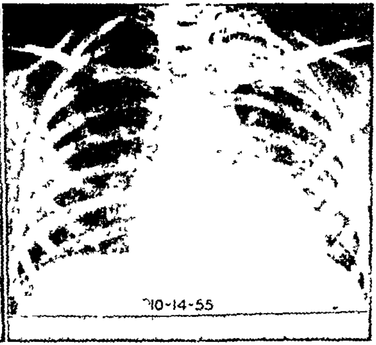

Fig 4

CASE 3—F. S, a 2 year old Negro boy, was admitted because of a large x ray density in the left upper lobe (Fig 6) Both foster parents were hospitalized for pulmonary tuberculosis Patch test was positive on admission All gastric and bronchial washings were negative for acid fast bacilli Chemotherapy was started and continued for a prolonged period since bilobar involvement was considered likely. Only moderate improvement occurred after 2 years of specific therapy. Apical posterior segmental resection was done on Oct. 30, 1956. The postoperative course was uneventful. The specimen contained large fibrocaseous lesions with severe bronchiectasis. Fig. 7 presents a follow-up x-ray examination 15 months after surgery.

Comment: This is an example of progressive primary disease with a persistent large caseous focus. It was believed that this represented a threat to the patient despite 24 months of chemotherapy.

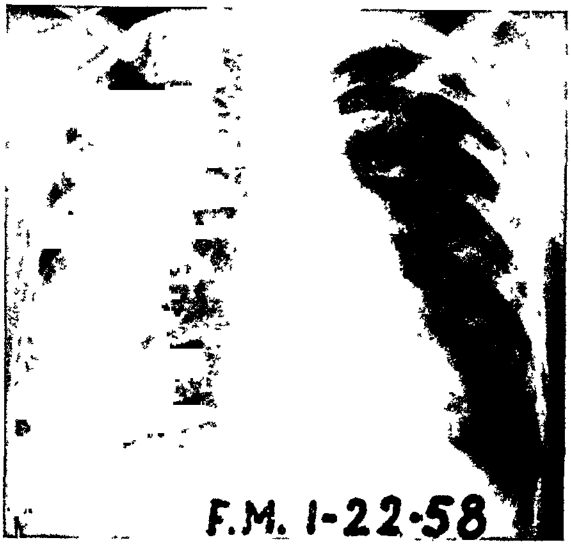

Fig. 5.

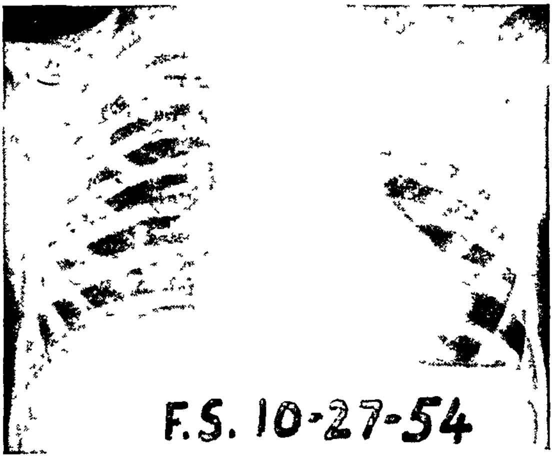

Fig. 6.

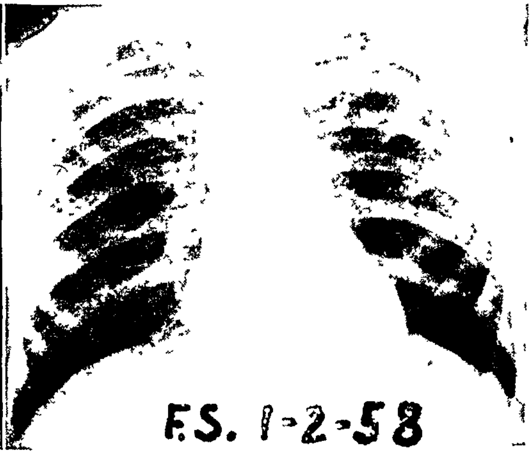

Fig. 7.

Case 4.—P. R., a 10-year-old Puerto Rican boy, was admitted because of fever, chest pain, and cough of 2 weeks' duration. Patch test, direct smear, and gastric washings (3×) were positive. Admission x-ray studies (*Fig. 8*) *demonstrated a large cavity in* the left upper lobe with bilateral bronchogenic spread. Chemotherapy was instituted with clinical and radiologic improvement. Bronchoscopy was negative. Tomography, after 15 months of treatment, revealed persistent cavitation in both upper and lower lobes on the left. Preoperatively (Fig. 9) the left lung appeared markedly contracted.

Pneumonectomy was performed on Jan 13, 1954, after 16 months of chemotherapy The postoperative course was uneventful Pathologic examination revealed a shrunken, fibrotic left lung with fibrocaseous and cavitary lesions in both lobes Fig 10 presents a follow up x ray examination made 3½ years after surgery

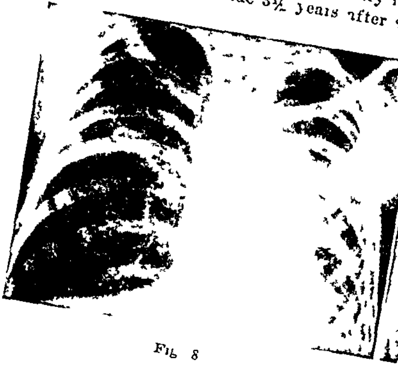

Fig 8

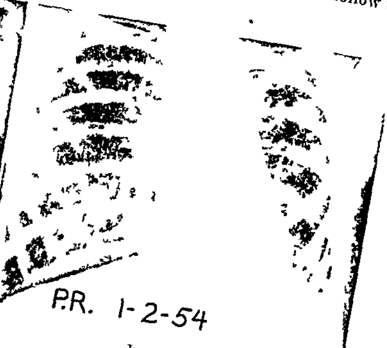

Fig 9

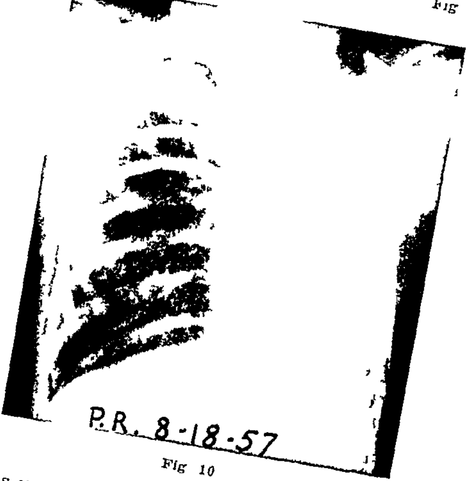

Fig 10

Comment This is a case of "destroyed" lung resulting from chronic pulmonary tuberculosis, reinfection type, uncontrolled after 16 months of chemotherapy The principal indication was that of persistent cavitary disease involving the entire contracted, functionally impaired lung

CASE 5—R L, a 13 month old Negro boy, was admitted with a history of cough, fever, and anorexia of 2 weeks' duration At 9 months of age the patient had had pneumonia which cleared slowly and was followed by frequent "colds" and intermittent fever. Admission Mantoux, gastric (6×) and bronchial washings were all positive. X-ray studies (Fig. 11) revealed clouding of the entire left lung field. After 5 weeks of specific chemotherapy, x-ray examination (Fig. 12) demonstrated a spread to the right.

Bronchoscopy revealed acute tuberculous endobronchitis of the left main-stem bronchus. Granulation tissue and caseous material, suggesting lymph node erosion, was observed. Cycloserine was added in the hope of controlling the endobronchial disease. Six months after admission, many high lights were seen in the previously opaque left chest.

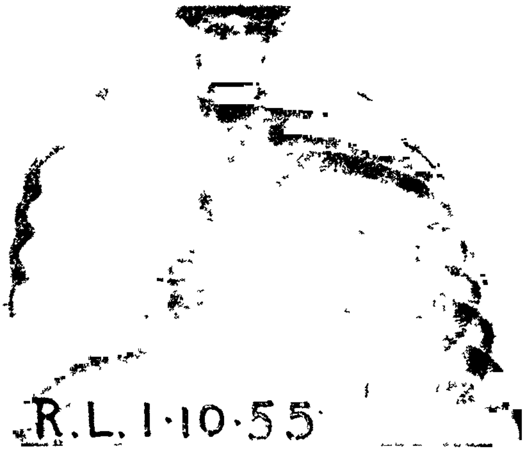

Fig. 11.

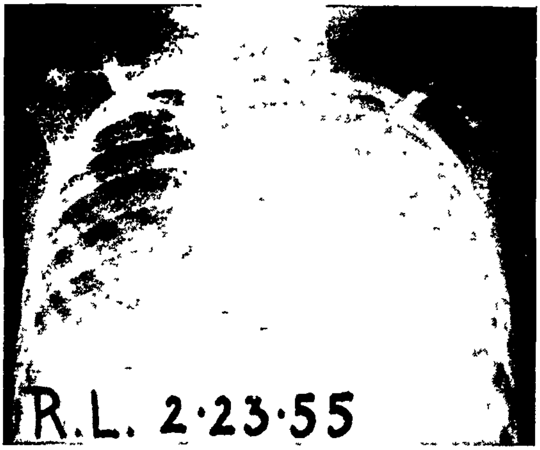

Fig. 12

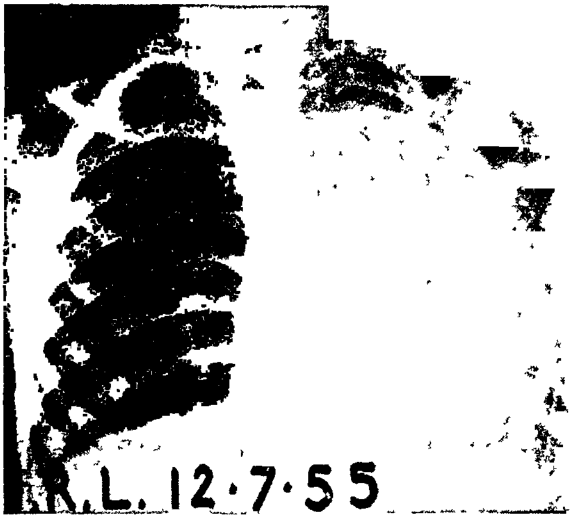

Fig. 13.

On bronchoscopy at this time, the main bronchus remained completely filled with granulation tissue. Serial bronchoscopic examinations during cycloserine therapy revealed gradual improvement. Eleven months after admission, x-ray examination (Fig. 13) again showed clouding of the entire left lung field with satisfactory clearing on the right. Pneumonectomy was performed with streptomycin coverage on Jan. 20, 1956, after a total of 12 months of chemotherapy. At operation the lung was found to be airless and contracted, and it failed to expand on positive pressure. The postoperative course was uneventful. The specimen consisted of a firm, shrunken lung crowded with saccular bronchiectasis and contained numerous small caseous nodules throughout.

Comment. This is an example of primary tuberculosis with endobronchial disease and rapid development of irreversible pathologic changes involving the entire left lung. Indication for surgery in this case was that of "destroyed" lung essentially post primary in nature. The diseased lung represented a threat to the patient from the standpoint of secondary nonspecific as well as possible specific infection.

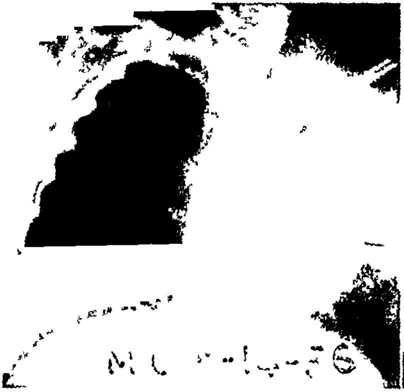

Fig. 14 A.

Fig. 14 B.

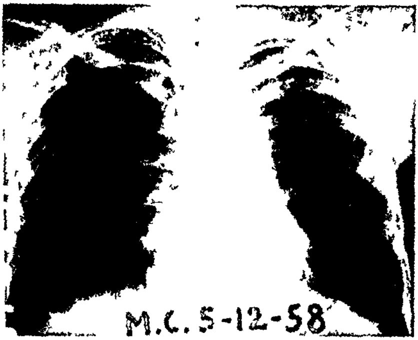

Fig. 15.

CASE 6.—M. C., a 6 year old Puerto Rican girl, was admitted with a history of cough, malaise and anorexia of 7 months' duration. X-ray studies revealed extensive nodular calcifications in the left upper lobe, more clearly seen on tomograms (Fig. 14, *A* and *B*). Gastric washings were positive. The patient was given specific therapy. Bronchoscopy showed tuberculous endobronchitis in the left upper lobe orifice which was observed to progress to bronchostenosis. The clinical course was marked by repeated bouts of bronchopneumonia thought to be due to intercurrent infection distal to the obstructed bronchus

Preoperative roentgenograms revealed only slight improvement. A left upper lobe lobectomy was done on June 27, 1957, after 10 months of chemotherapy. The postoperative course was uneventful. Extensive cavitation with peripheral calcification, pulmonary fibrosis, and bronchiectasis were found in the resected specimen. A follow-up x-ray study, 9 months after surgery, is presented in Fig. 15.

Comment: This is an example of large, nodular, calcified foci commonly referred to as "tuberculoma." Four of our patients had disease of this type. Three proved to have cavities, 1 uncontrolled caseous disease.

CASE 7.—M. C., an 8½-month-old Negro infant, was completely well until at the age of 5 months she was first hospitalized with pharyngotracheitis. Chest x-ray studies disclosed hilar lymphadenopathy. Subsequently, the child developed night sweats, recurrent upper respiratory infections, and episodes of wheezing respirations. The infant was readmitted to another hospital. Mantoux was positive. The patient was given specific chemotherapy and was transferred to our institution after about 40 days of treatment. On admission, x-ray studies (Fig. 16) disclosed marked bilateral hilar lymphadenopathy with evidence of obstructive emphysema in the right lower lung field. Specific antibiotic treatment was supplemented with steroid therapy. Five weeks later, x-ray examination (Fig. 17) revealed marked resolution of the hilar shadows and disappearance of the obstructive emphysema.

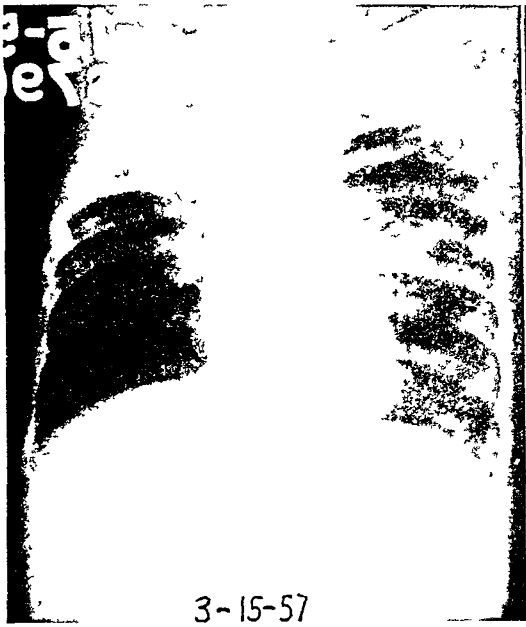

Fig. 16.

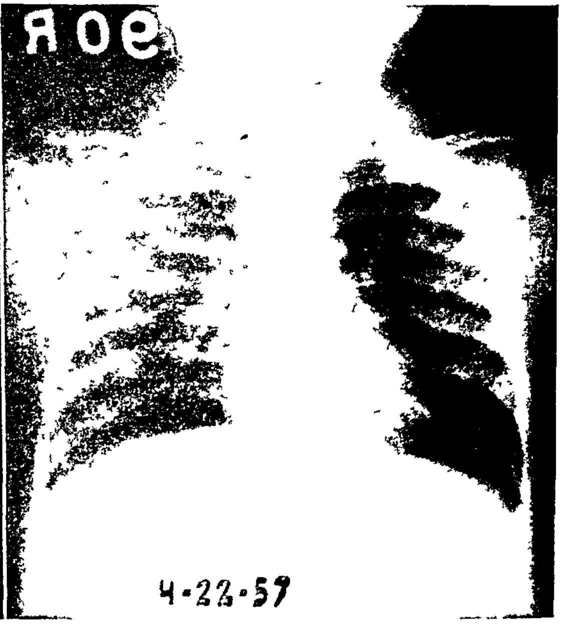

Fig. 17.

Comment: This is an example of acute hilar lymph node tuberculosis with endobronchial obstruction. It illustrates the improved response that may be anticipated with the use of steroids.

CASE 8.—D. B., a 2-year old Negro girl, had a history of cough and fever of 3 months' duration. These symptoms had developed after tonsillectomy. Patch test and gastric washings were positive. X-ray studies (Fig. 18) revealed a homogeneous density in the left mid-lung field which proved on lateral views to be in the superior segment of the left lower lobe. Tuberculous endobronchial disease was noted on bronchoscopy. Bronchial washings were positive for acid fast bacilli The patient was given specific chemotherapy and discharged to a sanatorium after 5 months of treatment with satisfactory response After 2 years of sanatorium care, the patient returned home improved More than a year later, the patient was readmitted to our institution after recurring episodes of infection during which physical signs were present in the area of the original disease Roentgenograms (Fig 19) showed a density in the left hilar area Bronchograms revealed saccular bronchiectasis in the superior segment of the left lower lobe (Fig 20, A and B) Gastric fluid was again positive for acid fast bacilli A resection of the superior segment, left lower lobe, was done on Oct 15, 1955 The postoperative course was uneventful Pathologic findings were predominantly those of bronchiectasis, fibrosis, and emphysema Direct smear was negative for acid fast bacilli

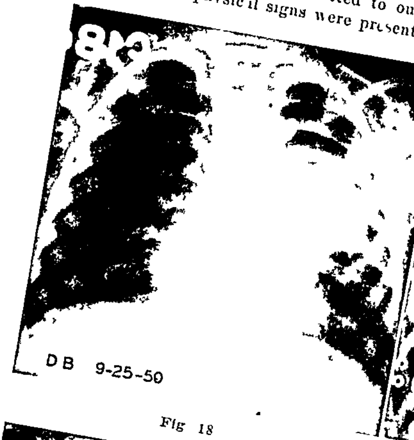

Fig 18

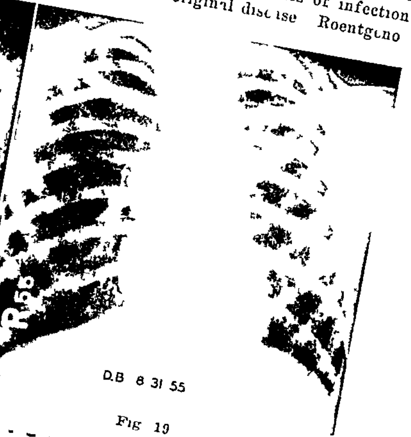

Fig 19

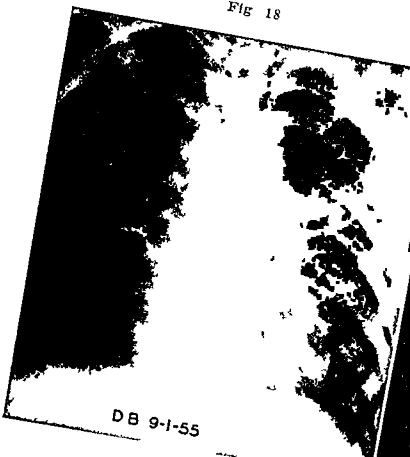

Fig 20 A

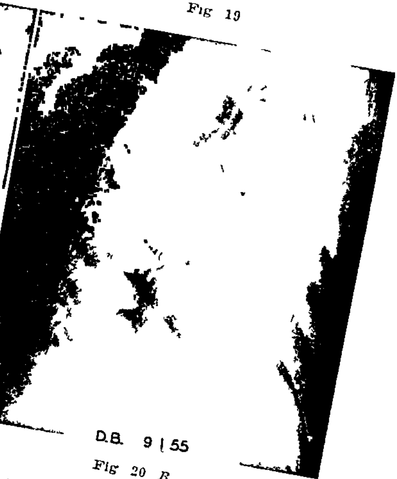

Fig 20 B

Comment: This is an example of segmental post-primary bronchiectasis resected 5 years after primary infection. Patient had recurrent infections in the involved area considered to be nonspecific. However, the gastric fluid obtained at the time of operation was reported positive for acid-fast bacilli.

Case 9.—R. J., a Puerto Rican boy, was first admitted to a sanatorium in Puerto Rico because of cervical, axillary, and inguinal adenopathy. Some of the cervical nodes were excised and were positive for acid-fast bacilli. At that time, chest x-ray studies revealed left hilar adenopathy with opacification of the left upper lobe. Sputum was positive. The child was given specific chemotherapy. Two years later, at age 9, the patient came to New York and was admitted to our institution with chief complaint of cough and malaise. X-ray examination (Fig. 21) showed a uniform density in the left upper lobe. Bronchoscopy revealed inflammatory reaction in the mucosa of the left upper lobe orifice. Gastric contents were positive. The patient was given specific chemotherapy and was discharged 14 months later. At that time, tomograms (Fig. 22) indicated the presence of a contracted, atelectatic left upper lobe. The child was readmitted for bronchograms and respiratory function studies. Bronchograms demonstrated left upper lobe bronchiectasis. Pulmonary function studies revealed decreased oxygen saturation at rest and after exercise. A left upper lobe lobectomy was performed on June 13, 1958, after 16 months of chemotherapy. The postoperative course was uneventful. Pathologic findings were those of bronchiectasis and fibrosis with scattered calcified nodules. Cultures were negative for acid-fast bacilli.

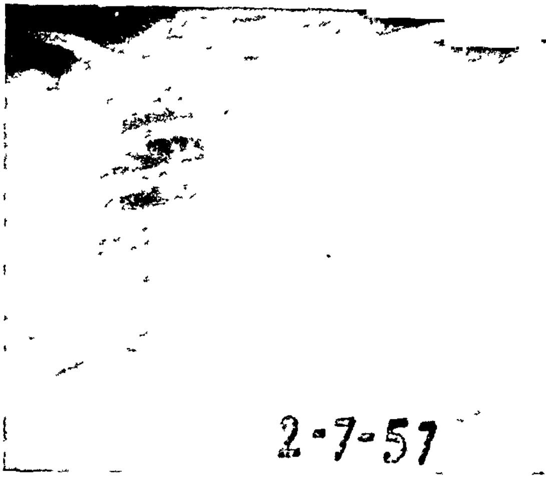

Fig 21

Fig. 22.

Table III summarizes the preoperative and postoperative respiratory function studies.

Table III. Respiratory Function Studies
(J.R. NR. 7278-55)

	PREDICTED	DETERMINED	
		PREOP.	POSTOP.
Vital capacity (L.)	1.75	1.90	1.70
Functional residual capacity (L.)	0.66	0.75	0.68
Residual volume (L.)	0.30	0.38	0.32
Total lung capacity (L.)	2.10	2.29	1.96
RV/TLC (per cent)	14.0	17.0	16.0
Maximum breathing capacity (L./min.)	50.0	45.0	54.0
A. B. O_2 saturation (per cent)	96+	86.0	99.0

Comment. This is an example of post-primary bronchiectasis and atelectasis. The patient was essentially asymptomatic. Functional studies provided the indication for surgery. The low arterial oxygen saturation (82 per cent) suggested that the diseased lobe functioned as a shunt. This was corrected by lobectomy.

Case 10.—M. McC., a white girl, was first admitted to our institution at 5 years of age. The patient's mother died of tuberculosis. Two sisters were admitted with the patient and another sister was previously hospitalized for tuberculosis. Patch test and

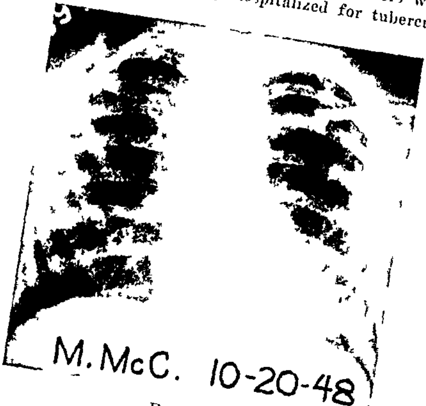

Fig. 23

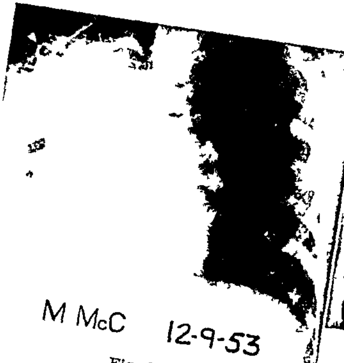

Fig. 24

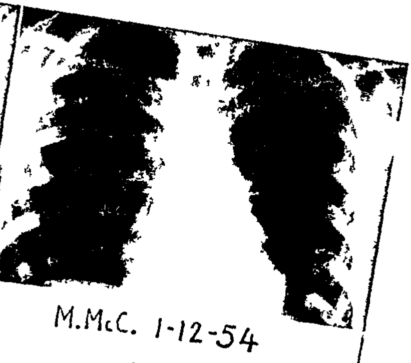

Fig. 25

gastric washings were positive (2×). A roentgenogram revealed a right upper lobe density (Fig. 23). Specific therapy was started and was continued after transfer to a sanatorium for a period of 10 months with good clinical response. She remained at the sanatorium for 2 years and was discharged improved. After discharge, the patient had an episode of pneumonia and hemoptysis but did fairly until she was readmitted at 10 years of age because of hemoptysis, cough, and fever of 4 days' duration. Roentgenograms were essentially the same as on first admission 5 years previously. A roentgenogram, one week after admission, shows a uniform density obscuring most of the right lung (Fig. 24). The patient was started on chemotherapy and the x-ray density cleared within a month (Fig. 25). Apical segmental resection was performed after 6 weeks of preoperative chemotherapy. The postoperative course was uncomplicated. The excised segment was markedly atelectatic and pathologic study showed fibrosis, bronchiectasis and nodular, partially calcified caseous disease.

Comment: This is an example of persistent segmental atelectasis. Resection was done because of recurrent hemoptysis after a 5-year period of observation.

CASE 11.—C. P., a 9-year-old white boy, was admitted because of bronchopneumonia. The patient had a positive patch test and x-ray evidence of a primary lesion at the age of 4. Subsequently, he was treated in a number of hospitals for recurrent pneumonitis which always cleared slowly. On admission to our institution, x-ray examination of the chest (Fig. 26) revealed a density in the left upper lobe with a calcified primary lesion. Sputum was consistently negative. The child was treated with antibiotics and discharged improved. After repeated episodes of respiratory tract infection, bronchograms (Fig. 27) revealed obstruction of the apical posterior segmental bronchus. The patient was readmitted and given specific chemotherapy. Preoperative x-ray studies showed considerable clearing of the parenchymal infiltrate. An apical posterior segmental resection was performed on June 16, 1952. The postoperative course was uneventful. The resected segment was fibrotic, atelectatic, and contained confluent areas of caseation necrosis. Direct smear and cultures were positive for acid-fast bacilli.

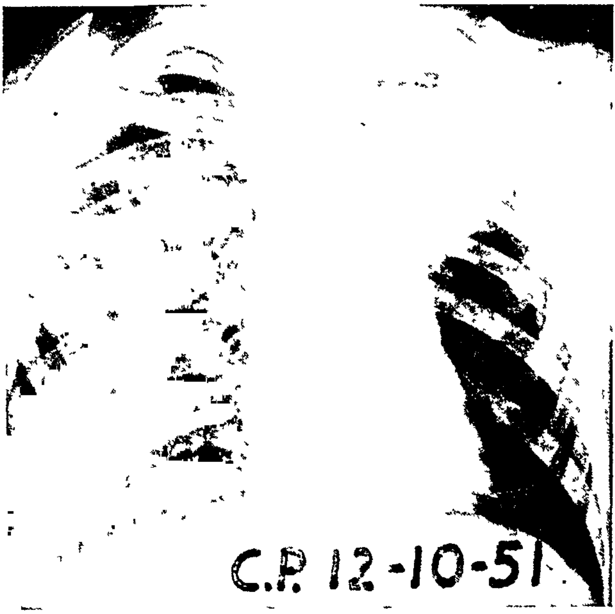

Fig. 26.

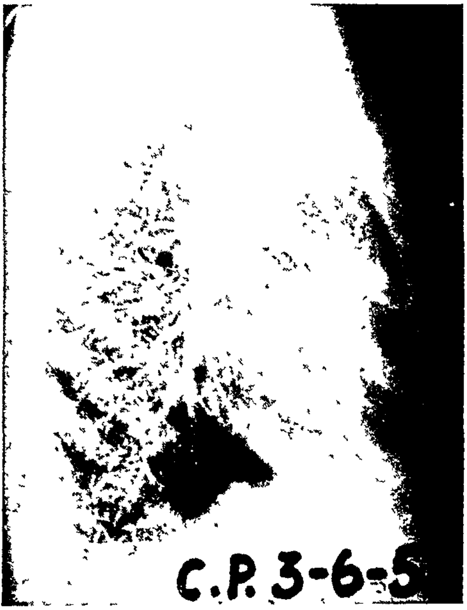

Fig. 27

Comment: This is an example of bronchial obstruction with tributary parenchymal atelectasis. Preoperatively, recurrent infection was considered to be nontuberculous in nature. It was undoubtedly specific since the resected specimen contained active caseous disease 5 years after primary infection.

CASE 12.—C. L., a 12-year-old Puerto Rican girl, was previously hospitalized for primary pulmonary tuberculosis during childhood in Puerto Rico. Chronic obstructive emphysema developed and she finally was sent to New York for possible treatment of this condition.

The patient was first admitted to another New York hospital. Specific chemotherapy was given for a period of 5 months because of a nodular density in the right upper lobe. The child was then transferred to our institution with right upper lobe emphysema and a nodular parenchymal lesion. Roentgenograms taken during expiration showed marked anterior herniation to the left. Bronchograms (Fig. 28) disclosed poor filling of the right upper lobe and downward displacement of the middle and lower lobes. Specific chemotherapy was continued and a right upper lobectomy was performed on Sept. 30, 1957, after 7 months of

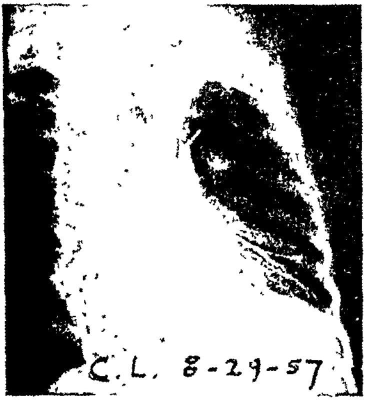

Fig. 28.

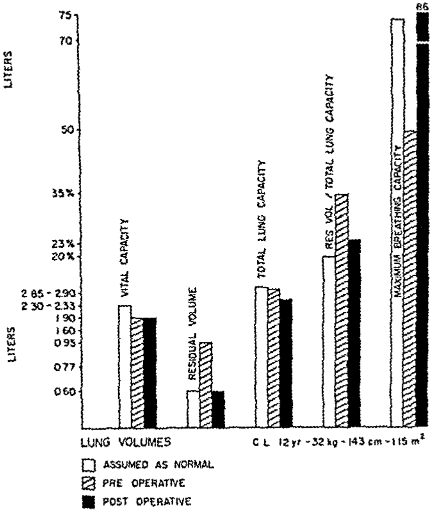

Chart 1

treatment. The postoperative course was uncomplicated. The resected lobe was markedly emphysematous, fibrotic, and bronchiectatic. There was uniform dilatation of all alveolar structures as is seen in congenital lobar emphysema in infancy. Findings of preoperative and postoperative functional studies are indicated in Chart 1.

Comment: This is an example of post-primary chronic obstructive emphysema. Functional studies, indicating the presence of increased residual volume and diminished maximal breathing capacity, were the essential indications for surgery. Function was markedly improved after lobectomy.

CASE 13.—H. H., a 12-year-old Negro boy, was well until 1 year prior to admission when he developed a left pleural effusion. He was admitted to another hospital where thoracentesis was performed. The fluid was negative for acid-fast bacilli on culture. Mantoux was strongly positive. Gastric washings were negative on smear but positive for acid-fast bacilli on guinea pig inoculation. Chemotherapy was instituted. The child improved clinically but the chest roentgenogram was unchanged and he was transferred to our institution. Admission roentgenograms of the chest (Fig. 29) revealed a homogeneous density on the left with contraction of the left rib cage and mediastinal displacement to the right. Steroid therapy was added with subsequent improvement. Three months later, there was still evidence of pleural thickening and restriction of the left rib cage. A roentgenogram, 10 months after admission (Fig. 30), showed continued improvement. Serial pulmonary function studies demonstrated constantly improving function as shown in Table IV.

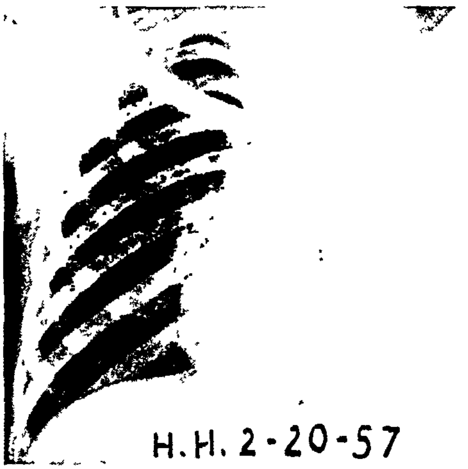

Fig. 29.

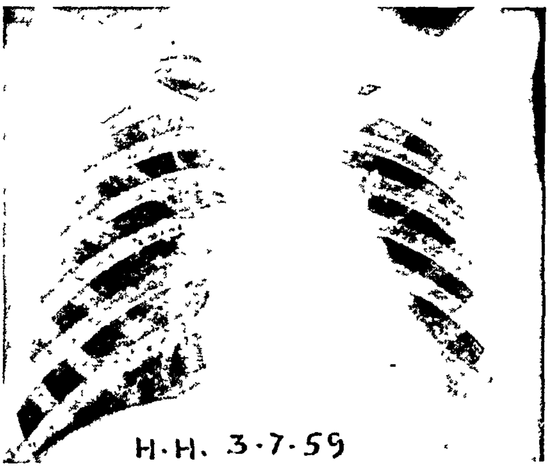

Fig. 30.

TABLE IV. LUNG VOLUMES
(H.H. NR. 8369-57)

		DETERMINED	
	PREDICTED	12/30/57	3/10/58
Vital capacity (L.)	2.3	1.3	1.6
Functional residual capacity (L.)	0.9	0.6	0.8
Residual volume (L.)	0.6	0.3	0.4
Total lung capacity (L.)	2.9	1.8	2.0
RV/TLC (per cent)	20.0	17.0	20.0
Maximum breathing capacity (L./min.)	60.0	30.0	50.0

Comment: This is an example of apparent "trapped" lung following a primary pleural effusion. The possibility of decortication was entertained at first However, physical findings, serial x ray studies, and fluoroscopic examinations, as well as functional studies, all indicated continually improving respiratory function and operation was not considered necessary

CASE 14—M M, a 7 year old white girl, was admitted because of an increased apical density in the right upper lobe This had first been noted 3 years previously The patient was a diabetic and had had 2 episodes of coma She improved clinically but showed little change in the roentgenographic density after 14 months of chemotherapy Apical and posterior segmentectomy was done on Oct 12, 1952 The postoperative course was uneventful Specimen revealed caseous, cavernous disease, positive for acid fast bacilli on smear

Comment This is an example of chronic pulmonary disease complicated by diabetes mellitus It was believed that the prognosis of the patient's pulmonary tuberculosis was affected adversely by the concomitant diabetes and that operation was more strongly indicated

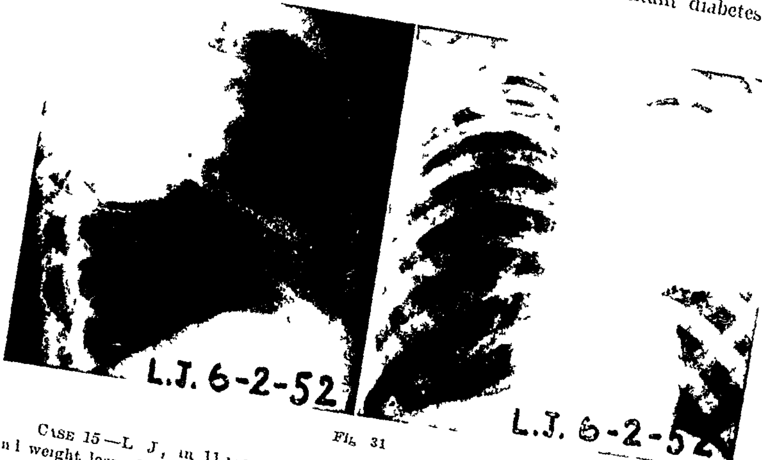

Fig 31

CASE 15—L J, an 11 year old Negro girl, was admitted with fever, cough, anorexia, and weight loss of 2 months duration Mantoux, negative 15 days prior to admission, became strongly positive on the day of admission Sputum was negative X ray studies (Fig 31) disclosed a large homogeneous density in the left upper chest which proved on lateral x ray studies to be in the superior segment of the left lower lobe Bronchoscopy revealed granulation tissue and caseous exudate suggesting an eroding node in the left lower lobe rific The patient was given specific chemotherapy with improvement Gastric and bron l al washings were positive for acid fast bacilli Left superior segmentectomy was l rf r n May 13, 1953 The immediate postoperative course was uncomplicated A l t l infiltrate over the left base was noted a few weeks postoperatively This l r hemotherapy Pathologic findings were those of tuberculosis of lung with n l lar caseous lesions lined by thin rims of fibrous tissue, bronchiectasis, and I l sis

an / This is an example of a well documented primary disease in t (11 years) There x-ray evidence of fairly go eal response to treatment. Nevertheless, it was believed that the approaching menarche and subsequent years of increased stress would influence the prognosis of a potentially caseous lesion unfavorably.

DISCUSSION

In the previous paragraphs the patients have been classified as having either reinfection or complicated primary tuberculosis. Chronic or reinfection tuberculosis tends to occur in older children. The clinical problems are similar to those observed in the treatment of adult patients. The indications for operation are commonly those first listed in Table II, Nos. 1 through 4. These are generally accepted and need no further comment.

The same indications apply as well to a smaller number of patients with progressive primary disease. This is prone to occur in the first years of life. There is less general agreement in advocating surgery at this time. It is known, however, that the prognosis of complicated primary disease is poorest in the 0 to 4 age group. Surgery may then be most strongly indicated. Twenty per cent of our patients were 2 to 5 years of age.

In our experience, excisional surgery and thoracic surgery, in general, are particularly well tolerated by younger children and infants. Thoracotomy results in less trauma to the more pliable chest cage. Ventilation is, therefore, not restricted by pain to the same degree as in older patients. There is less difficulty in maintaining a clear airway; lung expansion is usually prompt and complete.

The fifth indication deserves special mention. Marked deposition of calcium is characteristic of the healing response in infants and young children with progressive primary disease. Conglomerate calcified foci, sometimes referred to as "tuberculoma," may be erroneously regarded as controlled lesions. Excessive calcification may mask active disease (Cases 2 and 6).

The remaining indications, Nos. 6 through 10 (Table II), are more specifically related to the lymph node component of the primary complex and consequent post-primary complications. They present problems which are unique in the pediatric age group. The responsible pathologic factor is marked hilar lymphadenopathy—the outstanding characteristic of primary disease.

Endobronchial disease is directly related to hilar lymphadenopathy. Hilar lymphadenopathy noted in x-ray studies and endobronchial disease observed at bronchoscopy occur concomitantly. Our understanding of the causal relationship has been greatly enhanced by serial bronchoscopic studies. In a series reported from our clinic in 1952, the incidence of positive findings was extremely high. Almost all patients with endobronchial disease had a diagnosis of primary tuberculosis. Of the 43 patients with positive endobronchial findings, 42 presented evidence of obstruction. Thirty-seven had segmental or lobar atelectasis; 5 had obstructive emphysema. About 50 per cent of the patients with atelectasis had persistent shadows and in about 10 per cent bronchial stenosis developed Hilar lymphadenopathy is most pro nent in patients in the early months and years of life Although less th 50 per cent of the patients were under 3 years of age, this age group rep sented about 70 per cent of the observed endobronchial disease

Whereas the dreaded complications of primary tuberculosis, namel tuberculous meningitis and miliary tuberculosis, have been controlled wit the prompt and judicious administration of antibiotics, lymph node tuberculosis and its attendant bronchial complications usually do not have the same satisfactory response to antibiotic treatment

Acute hilar lymphadenopathy may require emergency surgical intervention Thoracotomy and excision or evacuation of nodes seriously compromising the airway have been reported In our experience the need for thoracotomy has not presented itself Acute respiratory symptoms may also result from erosion and spillage of caseous nodes in the bronchial lumen Bronchoscopic aspiration is then the most commonly indicated emergency treatment Aspiration of caseous contents and removal of obstructing granulation tissue have been performed in many of our patients More recently there has been an improved response in the treatment of acute lymphadenopathy and related endobronchitis with the combined use of antibiotics and steroid therapy (Case 7)

Thoracotomy for excision of nodes is also recommended by some authors as a prophylactic measure in asymptomatic patients with x-ray evidence of persistent bronchial obstruction either atelectasis or emphysema This practice does not seem justified since only a few of these patients will have permanent damage requiring excisional surgery

The late effects of hilar lymphadenopathy, namely, bronchiectasis, with or without bronchial stenosis, and persistent atelectasis are more pertinent in the discussion of our cases

Bronchiectasis and persistent atelectasis are closely related problems Bronchographic examination of atelectatic lung will in most instances reveal bronchiectasis In symptomatic bronchiectasis, recurrent infection and hemoptysis are common indications for operation Infection may be specific but is more commonly secondary nonspecific in nature Differential diagnosis is frequently difficult In clinically quiescent disease, tubercle bacilli are occasionally found if adequately sought for Active disease is sometimes an unexpected finding in resected specimens when preoperative bacteriologic examinations have been consistently negative Therefore, latent specific disease always remains a possibility

In asymptomatic bronchiectasis, especially with atelectasis, functional onsiderations are of paramount importance The involved lung may be use l ss as ventilating tissue and even detrimental when increasingly greater por ns of parenchyma are affected Respiratory function studies then provide prime indication for excisional surgery Elective surgery might be con ered in a few instances when the nature and location of asymptomatic se indicate a poor prognosis Middle and lower lobe involvement is nerally of more serious import Post primary middle lobe bronchiectasis, asymptomatic in childhood, is undoubtedly responsible in many instan adult "middle lobe" syndrome. Upper lobe involvement, often considered benign, has also been a source of late complications in a significant number of cases (Cases 10 and 11). Improvement in general health has been observed following resection of asymptomatic post-primary disease. It may then be assumed that the diseased tissue represented a focus of infection without obvious clinical manifestations.

Acute obstructive emphysema is observed quite frequently in the acute phase of primary lymphadenopathy. Chronic obstructive emphysema is an infrequent post-primary complication (Case 12). Respiratory function studies provide again the definite surgical indication.

Primary pleural effusion resulting in chronic pleuritis and impaired pulmonary function is frequently cited as an indication for thoracotomy and decortication. Decortication has often been done in conjunction with pulmonary resection, but has not been found necessary as a primary procedure in our experience (Case 13).

Secondary indications for surgery have been those of sex and age as well as the presence of concomitant systemic disease. Diabetes, for example, affects prognosis adversely and its presence further justifies surgical intervention. In some instances, factors of age and sex have influenced surgical opinion. An increased incidence of relapse has been observed at puberty and succeeding years so that resection of questionably stable lesions is advisable before the expected period of added stress.

The late results have been gratifying. In addition to the hospital mortality previously reported, one patient died of acute nonspecific pneumonitis 3 years after pneumonectomy for suppurative post-primary bronchiectasis. The remaining patients (38) are living and, to the best of our knowledge, are free of active disease.

SUMMARY

The prognosis of pulmonary tuberculosis in children has been altered favorably by the use of specific chemotherapy and has permitted the consideration of surgical treatment. Forty patients between 2 and 13 years of age were treated with pulmonary resection. The indications for surgery are analyzed and illustrative cases are presented.

The authors are deeply indebted for the advice and cooperation of Dr. Edith M. Lincoln, Adjunct Professor of Pediatrics, New York University College of Medicine and former Director of the Children's Chest Unit of the Medical Service of Bellevue Hospital; Dr. Margaret H. D. Smith, Associate Professor of Pediatrics, New York University College of Medicine and Director of the Children's Chest Unit of the Medical Service of Bellevue Hospital; Dr. John F. Daly, Professor and Chairman, Department of Otolaryngology, New York University Post-Graduate Medical School; and Dr. Juan Filler, Assistant Professor of Pediatrics, New York University College of Medicine and in charge of the Pediatric Cardiopulmonary Laboratory, Bellevue Hospital.

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adult "middle lobe" syndrome. Upper lobe involvement, often considered benign, has also been a source of late complications in a significant number of cases (Cases 10 and 11). Improvement in general health has been observed following resection of asymptomatic post-primary disease. It may then be assumed that the diseased tissue represented a focus of infection without obvious clinical manifestations.

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DISCUSSION

DR WILLIAM M LEES, Chicago, Ill —You heard Dr Fox a few minutes ago confirm the work that was done at a sanatorium 25 miles away from the Municipal Tuberculosis Sanitarium in Chicago, and I am now about to discuss the results at a sanitarium 900 miles away with almost identical results, and I should like to state that Dr Fischer did not bribe me to make these comments

We are happily surprised that their problems and results are identical with ours We, too, have had 40 resections in children, 8 of these prior to 1953 None of these 8 received isoniazid Since that time, all of the children received isoniazid, and there were neither major complications nor deaths in this group We had deaths in the earl of children, one of cardiac asystole just as the hilar dissection was begun; one following a pneumonectomy in a teenage girl who had a massive spread of disease to the remaining lung.

I should like, then, to show two representative cases.

This slide will demonstrate the chest films of a 12-year-old Negro girl who was admitted to our sanitarium with pneumonic disease (slide), as you see in the left upper slide. The slide on the right shows the ultimately destroyed left lung. A pneumonectomy was performed on this patient in June of 1950. There was a minor spread in the right upper lobe which cleared on chemotherapy. She is now married and has a child.

The next slide demonstrates a patient very similar to the one Dr. Fischer demonstrated. This is of a youngster 19 months of age who had a left upper lobe pneumonic lesion which partly cleared to leave a solid appearing 3 cm. nodular lesion which had an eggshell consistency at the time of the apical posterior segmentectomy. This proved to be a 2.5 cm. cavitary lesion from which caseous debris shelled out readily.

I therefore should like to completely confirm what Dr. Fischer said, and I would like to summarize our impressions as follows: (1) we believe children withstand this surgery quite well; (2) they are more alert; (3) they are less sensitive to pain postoperatively; (4) they cough better; (5) handle their secretions better; (6) they take anesthesia much better than some of the adult patients we have had; (7) they are more quickly and more vigorously ambulatory after operation; (8) their recovery period is much shorter, and (9) the resiliency of the infant's and young child's lung is such that we have not encountered any space problems. We therefore completely agree with what Dr. Fischer has told you.

DR. FRANCIS H. COLE, Memphis, Tenn.—I would like to report in from further south, Memphis, Tennessee, where we also have had a similar experience to that reported by Dr. Fischer. We have had the opportunity as well to operate, with very gratifying results, upon one child who was in acute respiratory distress from mediastinal lymphadenopathy.

In our children we have had 49 operations in 43 patients. One of the patients is dead; the others are all alive and have no evidence of residual disease.

DR. CONSTANTIN G. CHARONIS, Baltimore, Md.—I too would like to compliment Dr. Fischer for his fine work. I arise merely to pose one question which can be considered a free consultation requested by a Resident in Thoracic Surgery.

Did you encounter severe mediastinal shifting accompanying a persistent dry pleural space following pneumonectomy in children or adolescents?

Two teenagers among our young patients developed this complication following pneumonectomy. Repeated regulations of the intrathoracic pressure have been necessary since. In 1 of these 2 patients, phreniclasia was done a few months postoperatively with rather poor results concerning the mediastinal shifting. We have employed the Wilms-Saurbruch thoracoplasty only in adult patients developing the above complication, with satisfactory results.

Can you please comment on the treatment of the above complication in children and adolescents?

DR. FISCHER (Closing).—I wish to thank the discussers.

I would reiterate what Dr. Lees said in regard to postoperative complications. In general, children tolerate thoracic surgery exceedingly well and have less postoperative difficulty than adults. Thoracotomy results in less trauma to the more pliable chest wall of younger patients. They, therefore, experience less chest wall pain and do not have as much difficulty maintaining a clear airway postoperatively. Complications are therefore relatively infrequent.

In regard to Dr. Charonis' question concerning mediastinal shift, we have not used thoracoplasty after either partial or total resection. The pneumonectomy patients do not have clinical evidence of impaired pulmonary function. In those who have had postoperative respiratory studies the observed function may be as high as 80 per cent of the predicted normal.

PERSISTENT PLEURAL AIR SPACE FOLLOWING RESECTION FOR PULMONARY TUBERCULOSIS

T. W. Shields, M.D. (by invitation), Wm. M. Lees, M.D.,** R. T. Fox, M.D.,*** and G. Salazar, M.D.**** (by invitation), Chicago, Ill.*

A PERSISTENT pleural air space following resection for pulmonary tuberculosis has been encountered more frequently in recent years. Many of these spaces are completely benign while others become a serious postoperative complication and occasionally may result in death. Since the persistent air space is potentially hazardous, various procedures such as preoperative or concomitant thoracoplasty, "lung reconstitution,"[1] "pleural tent,"[2] "diaphragmatic advancement,"[3] etc., have been advocated to prevent its occurrence. However, universal acceptance of any one of these procedures has not occurred indicating that the problem is as yet unsolved.

A review of this complication following pulmonary resection has been carried out at the Chicago Municipal Tuberculosis Sanitarium in an attempt to elucidate some of the factors concerned with its development and control. Also, clinical guides were sought for the early differentiation between the benign space and the potentially hazardous one.

METHOD OF STUDY

The postoperative roentgenograms of all tuberculous patients undergoing pulmonary resection, except pneumonectomy, from Jan. 1, 1955, through Dec. 31, 1957, were reviewed. Any air space persisting 2 weeks or longer after the operation or requiring additional active therapy other than the chest drainage employed routinely following surgery was included in the study. The clinical records of these patients were then reviewed and all pertinent data were tabulated. One- to 3-year surgical follow-up examinations were made.

The pulmonary resections were classified into four groups: subsegmental resection (wedge), segmentectomy, lobectomy, and lobectomy plus additional resection of adjacent lung tissue. Each was accomplished through a standard

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****Resident in Surgery, Municipal Tuberculosis Sanitarium, Chicago.

posterolateral thoracotomy incision. The Lees wedge clamps were utilized for the subsegmental resection and the cut surface of the lung was closed with running sutures. The segmentectomies and lobectomies were accomplished by the standard hilar dissection and individual ligation technique. The raw surfaces of the lung when present were left open. The bronchial stump was closed with interrupted fine silk sutures. A pleural flap was used to cover the stump routinely when a lobectomy was performed and occasionally with segmentectomy. Drainage of the pleural space was routinely carried out with two large intercostal catheters attached to water-seal bottles. Immediate or late suction was employed in almost all cases. The chest tubes were removed when the drainage was less than 50 c.c. per 24 hours and an air leak was no longer present. Postoperative chest roentgenograms were taken at frequent intervals.

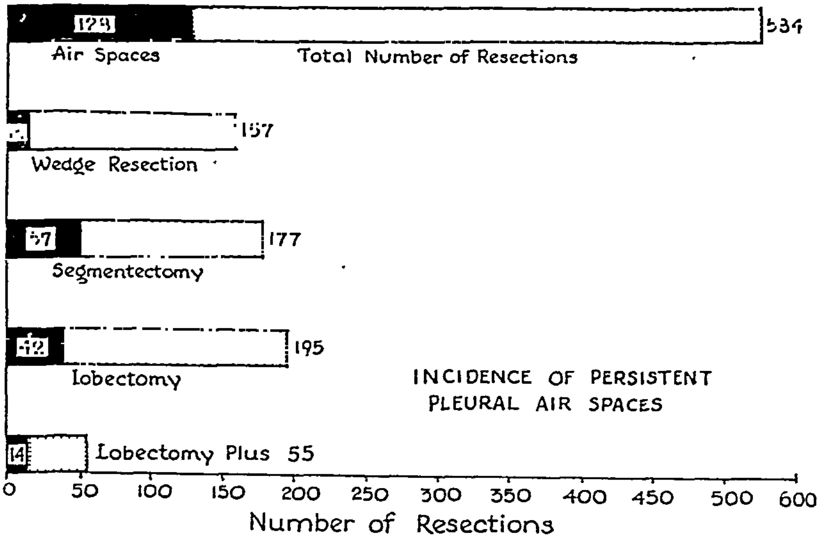

Fig. 1.—Incidence of persistent pleural air spaces following resection for pulmonary tuberculosis.

RESULTS

Incidence.—During the 3-year period of study, 584 resections (other than pneumonectomies) were performed. Of these, 157 were subsegmental resections, 177 were segmentectomies, 195 were lobectomies, and 55 were classified as lobectomies plus additional resection of adjacent lung (wedge, segment, or lobe). The review of the postoperative chest roentgenograms in each revealed the occurrence of 128 (21.9 per cent) persistent pleural air spaces.

Fifteen (9.5 per cent) of the spaces followed wedge resection, 57 (32.2 per cent) followed segmentectomy, 42 (21.5 per cent) occurred after lobectomy, and 14 (25.4 per cent) were seen after resection of a lobe or more (Fig. 1).

With the exception of those air spaces following lobectomy, the air spaces occurred with approximately equal frequency on the right and left sides. In the lobectomy group, 37 persistent air spaces were seen after 134 resections on the right and only 5 spaces after 61 resections on the left.

The 128 air spaces occurred in 125 individuals. The youngest was 15 years of age and the eldest 58, with the majority of individuals being in the third and fourth decades. Seventy-four were women and 51 were men. Eighty-five patients were Caucasians, 39 were Negroes, and 1 was of Oriental descent.

Clinical Classification of Space.—In reviewing the records it seemed advisable to classify each space into one of two groups: symptomatic or asymptomatic. The asymptomatic group included each air space in which the clinical course of the patient was unaffected by its presence with respect to symptomatology or clinical well-being. The symptomatic group included the air spaces which were judged to be the cause of postoperative symptoms such as pain, dyspnea, hemoptysis, fever, or continued air leak, and required operative intervention of varying magnitude for the control of the complications.

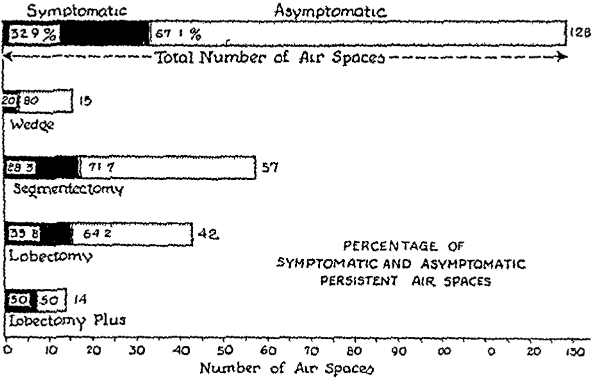

Fig. 2.—Incidence of symptomatic and asymptomatic pleural air spaces.

Utilizing these criteria, 86 (67.1 per cent) of the 128 air spaces were determined to be asymptomatic, and 42 (32.9 per cent) were classified as symptomatic. The incidence of the asymptomatic and symptomatic spaces in the four types of resection is seen in Fig. 2. It is to be noted that as the magnitude of the resection increased the percentage of symptomatic spaces likewise increased.

Preoperative Status.—All patients in both the asymptomatic and symptomatic group were judged to have reached clinical and roentgenographic stability of their disease process. Each had received streptomycin, para-aminosalicylic acid, and isoniazid for 4 months or more prior to the surgical intervention. The sputum was positive in 4 patients who developed asymptomatic spaces and in 10 patients who developed symptomatic spaces. Acute endobronchitis previously had been present in 11 of the asymptomatic group and in 8 of the symptomatic group. However, tuberculous endobronchitis was discovered in the cut surface of the bronchus in the resected specimen in 3 of the latter group. Diaphragmatic paralysis due to previous phrenic nerve operation was present in 2 of the patients and a thoracoplasty was present in 4 patients in the symptomatic group; in each of the latter the indication for resection was failure of the thoracoplasty to control the patient's disease.

At the time of surgery, a phrenic crush was utilized 3 times and one concomitant thoracoplasty was performed. No other methods to reduce the size of the pleural space were carried out at the time of operation.

Symptomatology and Complications.—By definition, demonstrable symptomatology and complications were absent in the 86 instances of asymptomatic air space. Eighty-three of these became apparent on the chest roentgenograms during the first postoperative week and the remaining 3 became evident during the second week.

This is in contrast to the symptomatic spaces. Only 27 of these 42 appeared during the first week, 12 were first recognized during the second week, and the remaining 3 were not demonstrable until the third postoperative week. One or more symptoms or signs, interpreted as being related to the persistent air space, were present in each of the 42 patients. These were prolonged temperature elevation or septic type of temperature course in 26; irritative cough productive of blood-streaked, frankly bloody, or purulent sputum in 23; continuous air leak in 13; a sensation of pressure or tightness in the chest in 11; dyspnea in 2; and the early roentgenologic appearance of a fluid level in the air space in 2 patients.

The complications that occurred (Table I) were bronchopleural fistula with empyema in 15 patients, bronchopleural fistula without overt empyema in 3, and empyema alone in 3. A partial pneumothorax occurred in 9 patients after previous complete expansion of the lung and a tension pneumothorax developed in 1 patient. A persistent peripheral air leak (alveolar pleural fistula) was present in 8 patients and "pseudocavity"[4] developed in the remaining patient.

TABLE I

COMPLICATIONS OF SYMPTOMATIC AIR SPACES	
Bronchopleural fistula	18
Delayed pneumothorax	9
Persistent peripheral air leaks	8
Empyema	3
Tension pneumothorax	1
"Pseudocavity"	1

Treatment.—In any patient who appeared to demonstrate slow or poor re-expansion of the remaining lung on the operative side, a pneumoperitoneum was routinely instituted early in the postoperative period. Consequently, this procedure has not been considered as an additional therapeutic measure in the present study. Despite the eventually proved benignity of the asymptomatic space, active treatment to obliterate the space was occasionally carried out. Needle aspiration was performed in 5 patients and a tube thoracostomy with water-seal drainage was likewise carried out in 5. A phrenic crush was done in 1 patient.

The treatment of the symptomatic spaces, on the other hand, involved many procedures and often taxed the ingenuity of the surgical staff. In those patients having a delayed pneumothorax or a persistent peripheral alveolar leak, aspiration or a closed tube thoracostomy generally was sufficient. However, in the patients with a large caliber leak (bronchial leak), multiple procedures were frequently necessary. A total of 71 procedures (Fig. 3), including multiple aspiration, closed tube thoracostomy, thoracoplasty (extraperiosteal plombage, conventional or Schede), open drainage, secondary bronchial closure, additional, resectional surgery, and silver nitrate cauterization of the bronchial fistula, was carried out in 41 patients. In the remaining patient, a small bronchopleural fistula healed without operative intervention.

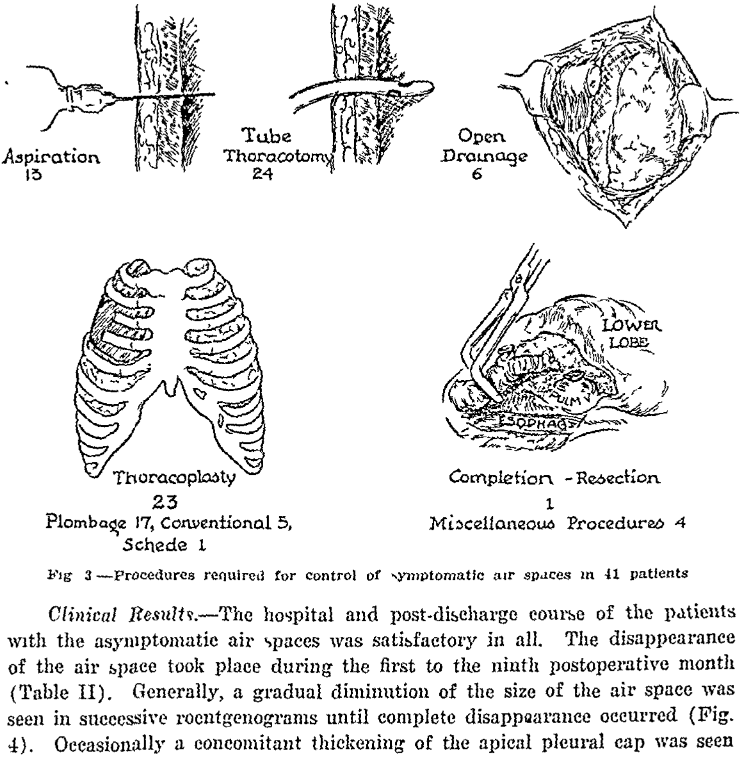

Fig 3.—Procedures required for control of symptomatic air spaces in 41 patients

Clinical Results.—The hospital and post-discharge course of the patients with the asymptomatic air spaces was satisfactory in all. The disappearance of the air space took place during the first to the ninth postoperative month (Table II). Generally, a gradual diminution of the size of the air space was seen in successive roentgenograms until complete disappearance occurred (Fig. 4). Occasionally a concomitant thickening of the apical pleural cap was seen during this period (Fig. 5).

In the 42 individuals with the symptomatic spaces the eventual outcome was satisfactory in 38 patients (Fig. 6 and Fig 7), unsatisfactory in 1 (persistent bronchopleural fistula), and death in 3 patients. Each of these patients died of the complication of a bronchopleural fistula. Two succumbed in the first postoperative month as a result of insufficient pulmonary reserve. The third present in 2 of the patients and a thoracoplasty was present in 4 patients in the symptomatic group; in each of the latter the indication for resection was failure of the thoracoplasty to control the patient's disease.

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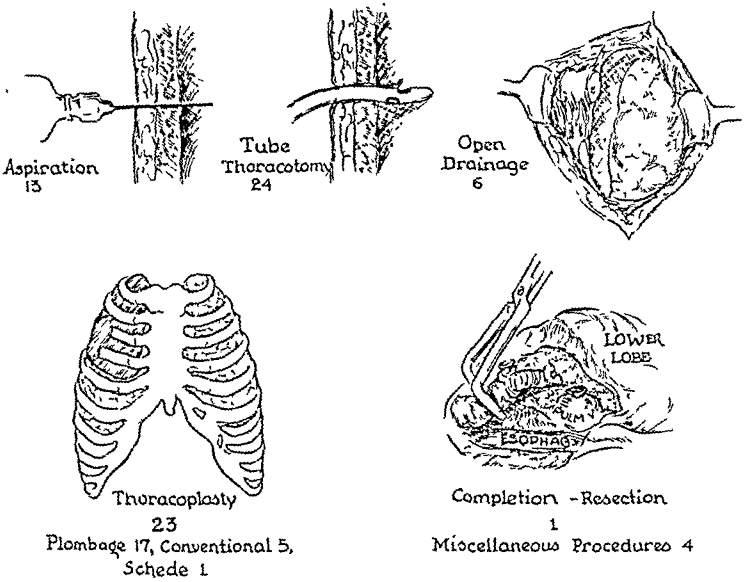

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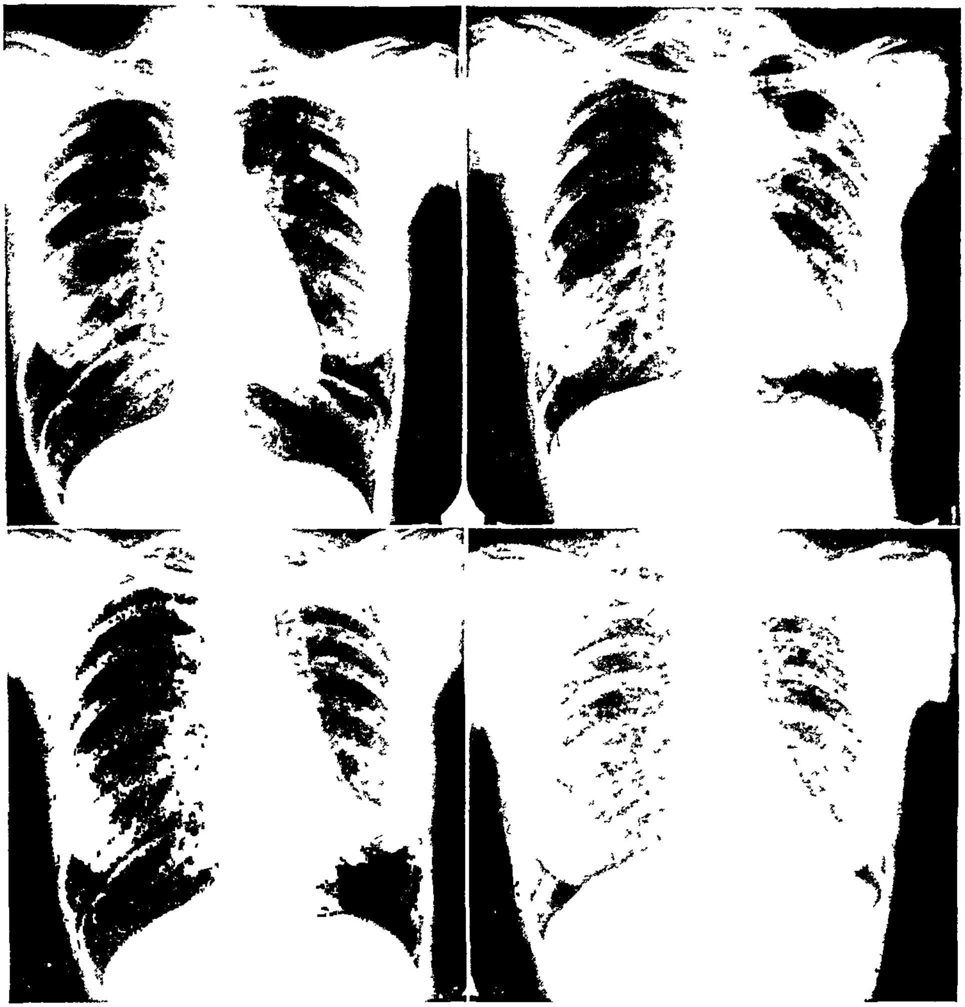

Fig. 4.—Asymptomatic air space following left apicoposterior segmentectomy.
A, Preoperative chest roentgenogram (Sept. 4, 1956.)
B, Air space present 19 days postoperatively. (Sept. 24, 1956.)
C, Air space has shown gradual decrease in size; no active treatment. (Nov. 13, 1956.)
D, Complete disappearance. (May 22, 1957.)

TABLE II. TIME OF DISAPPEARANCE OF AIR SPACES*

MONTH	ASYMPTOMATIC	SYMPTOMATIC
1	12	10
2	26	11
3	15	6
4	12	1
5	6	1
6	7	1
7-12	7	7
Over 13	0	2
Unknown	1	

*Excluding three deaths.

fistula. As a last resort to contral the fistula, a right pneumonectomy was performed and the patient succumbed in the first 24 hours of hemorrhagic diathesis.

In the 38 patients, in whom the result was eventually satisfactory, obliteration of the symptomatic space was accomplished during the first to the eighth month in 37 and by the fourteenth month in the remaining patient (Table II).

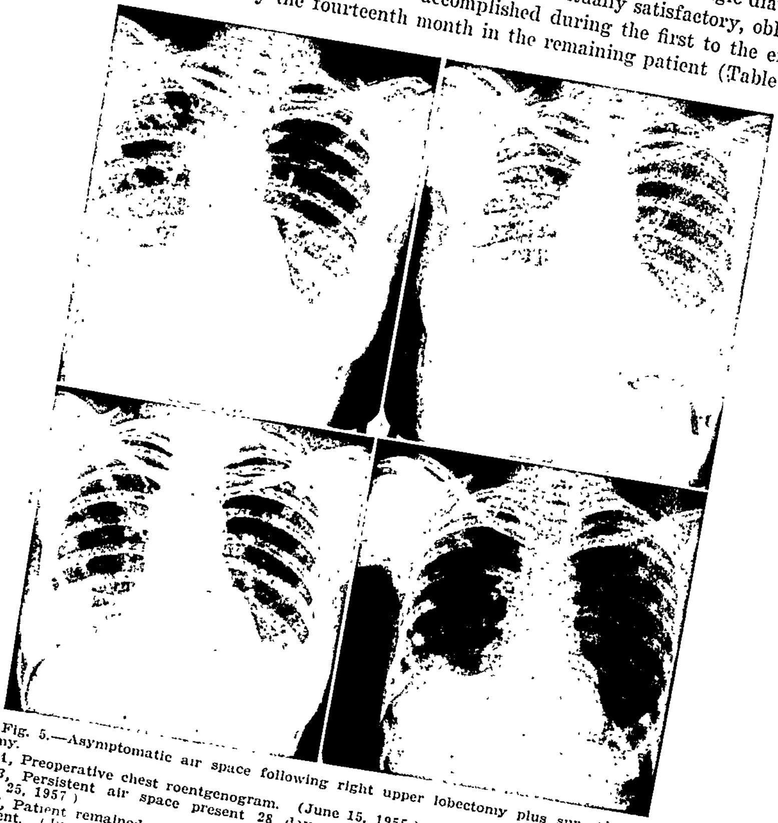

Fig. 5.—Asymptomatic air space following right upper lobectomy plus superior segmentectomy.

A, Preoperative chest roentgenogram. (June 15, 1955.)

B, Persistent air space present 28 days postoperatively. Pneumoperitoneum present. (April 25, 1957.)

C, Patient remained asymptomatic with slow disappearance of air space with no active treatment. (June 3, 1957.)

D, Final complete re-expansion (note small apical cap). (Oct. 7, 1957.)

DISCUSSION

In reviewing postoperative problems in resectional surgery for tuberculosis prior to 1952 and those of nontuberculous patients, we find no similar incidence of persistent peripheral air leaks and pleural air spaces as seen in the tuberculous patient today. In analyzing the possible factors which might explain this discrepancy, a comparison of the morphologic pattern of the resected tuberculous tissue of recent years with that of specimens of earlier years and that of nontuberculous lungs may be helpful. Such a comparison[5] shows that there had been a definite change in the fibrous and elastic tissue pattern in the tuberculous lung recently. There is a diffuse increase in fibrous tissue in the perivascular and septal spaces; and in the regions where necrosis has occurred, fibrous proliferation has taken place earlier and more extensively than a few years ago. Even in portions of the lung apparently uninvolved in the tuberculous process, as determined by roentgenographic or palpatory examination, one finds varying degree of similar interstitial fibrous proliferation. These changes have

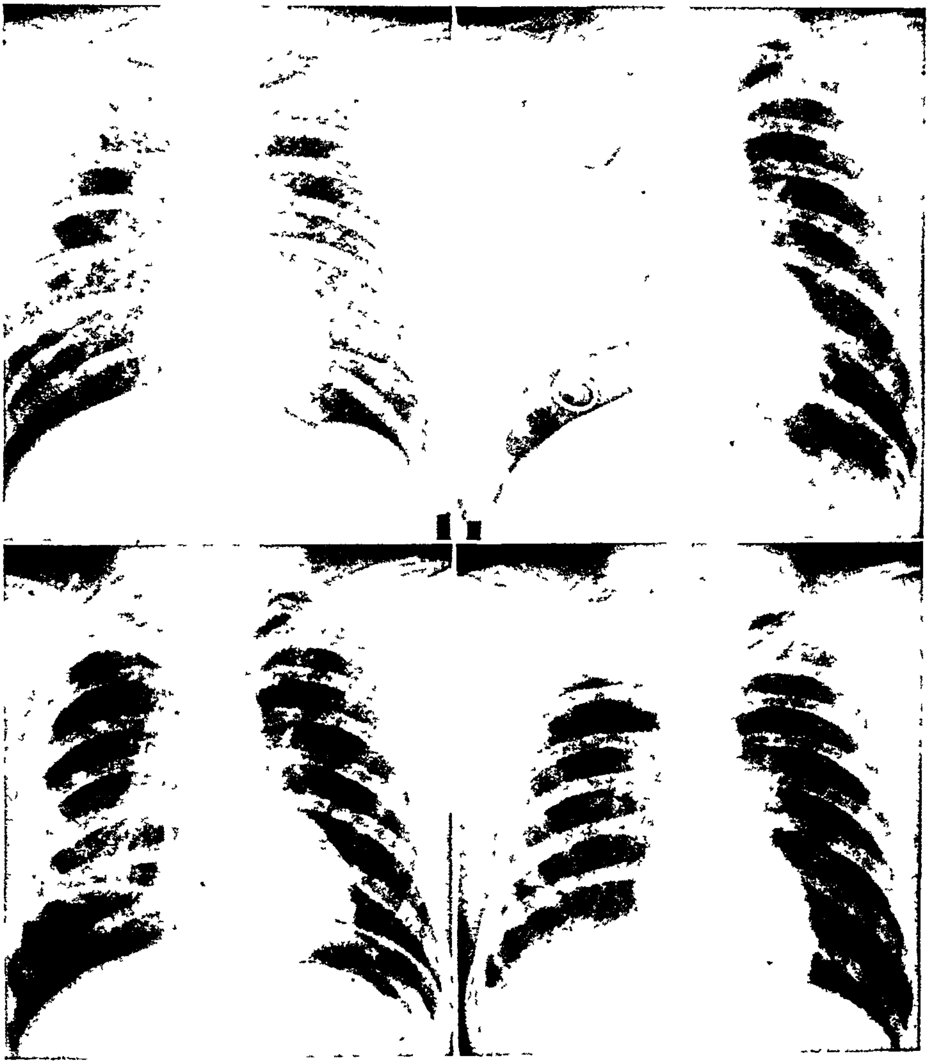

Fig. 6.—Symptomatic pleural air space following right upper lobectomy.
A, Preoperative chest roentgenogram. (June 15, 1955.)
B, Complete re-expansion with tube still in place. (June 23, 1955.)
C, Delayed pneumothorax. (June 28, 1955.)
D, Complete re-expansion following closed tube thoracostomy. Apical cap present. (Sept. 13, 1955.)

been noted by others[6, 7, 8] and it has been speculated that the use of antimicrobial agents has been the responsible factor. Isoniazid especially has been suspected in this regard. Irrespective of its cause, however, this fibrosis with the resulting interference with the normal elasticity and resilience of the lung tissue may explain the frequency and persistence of peripheral air leaks following resectional procedures. The persistence of such leaks is [illegible] the major cause of failure of the lung to re-expand with the resultant pleural air space.

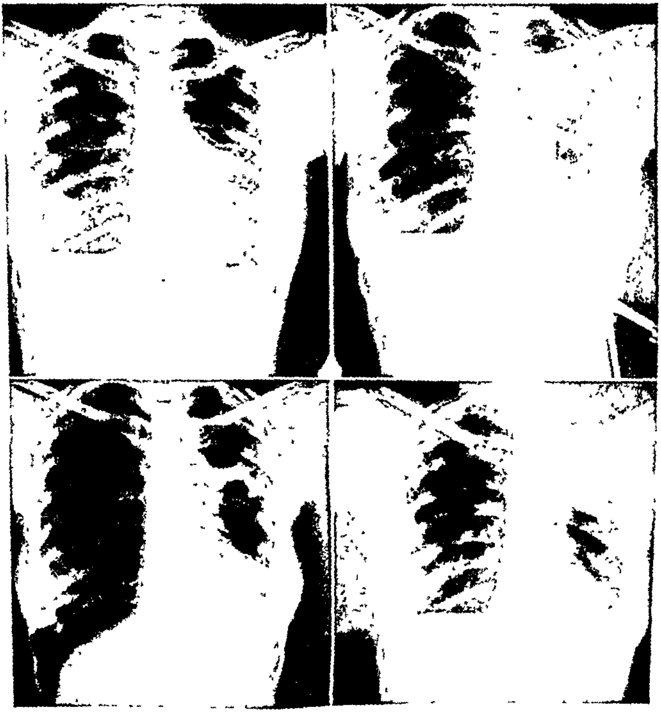

Fig 7—Symptomatic air space following left upper lobectomy and wedge resection of superior segment, left lower lobe.

A, Preoperative chest roentgenogram (Aug 27, 1956.)

B, Symptomatic air space (chills and fever). Closed tube thoracostomy has been performed (Sept 10, 1956.)

C, Failure of re-expansion with suction drainage. Bronchopleural fistula present. (Sept 24, 1956)

D, Obliteration of space following thoracoplasty with [illegible] (Nov 9, 1956)

In addition to such a true peripheral [illegible] air leak, a continuous or at least intermittent leakage of air from the [illegible] may [illegible]

This may either be from a true bronchial fistula due to inadequate healing of the bronchial stump or leakage from a thin-walled, dilated (bronchiectatic), peripheral, bronchial radical injured during removal of an adjacent segment or lobe. Either may be implicated in some of the patients as the cause of the persistent space. The bronchial fistula is an often-discussed hazard in resectional surgery and has been reduced to a minimum incidence of 3 to 5 per cent using currently accepted techniques. In the present series it was 3.1 per cent. Though these accounted for 14 per cent of the space problems and were the cause of the major morbidity and the only fatalities in the present series, a detailed discussion of this problem is not our purpose at this time.

The more peripheral bronchial and alveolar leaks are the ones that seem to be the factors causing the current increase in space problems. The relatively high incidence following segmentectomy (32.2 per cent) would indicate that intersegmental stripping produces a raw surface with many air leaks. The similar high incidence following right upper lobectomy (27.6 per cent) in contrast to left upper lobectomy (8.1 per cent) would seem to bear out this conclusion, inasmuch as the right upper lobe is so frequently fused to the middle lobe and requires extensive stripping during removal. Closure of these raw surfaces by such techniques as "lung reconstitution," as advocated by Bell,[1] is appealing as a potential solution but has not been successful in our hands. When persistent air leak from the raw surface occurs, achieving prompt reexpansion of the lung and obliteration of the pleural space is mandatory. Whether this is accomplished by vigorous suction alone or by concomitant reduction of the size of the pleural space must be left to the preference of the surgeon. Although the use of pleural tents, concomitant thoracoplasty, and other methods may be of some benefit we have used them infrequently. It appears from the above observations that the persistent air space will continue to be encountered and thus a rational plan of treatment must be evolved.

In the management of the postoperative air space, it would be of considerable help to the surgeon to be able to predict with relative certainty which space will disappear without active treatment and which will need some form of operative intervention. Early recognition and vigorous management of the latter might greatly shorten the convalescence, prevent major morbidity or even death, and possibly minimize any additional ventilatory function loss. Any air space occurring in a patient with a positive sputum or which reveals histologic tuberculous endobronchitis of the cut end of the resected bronchus is potentially dangerous. Also, the greater the extent of resection the more suspiciously must a persistent space be viewed. Prolonged fever, persistent bubbling from the drainage tubes, continued bloody or purulent expectoration, and especially roentgenographic appearance of the space later than the first week, or an air fluid level in the space connote trouble impending or already present. Any of these indicate the need for prompt institution of appropriate therapy. Lacking any of the above, a course of watchful waiting can be pursued with relative confidence of a successful disappearance of the space without complication.

When active treatment is indicated, although individualization must be applied, a routine series of procedures is followed in most cases In the first 2 or 3 days postoperatively, if re expansion is not satisfactory, a pneumoperitoneum is instituted or, if one was present preoperatively, refills are begun and continued until re expansion is complete If the air space persists and becomes symptomatic or appears after the removal of the drainage tubes, needle aspiration of the space is performed and pressure measurements are made If a negative pressure cannot be maintained with aspiration, then a closed tube thoracostomy is performed and continuous suction is applied

If the air leak still persists and re expansion does not occur, the intercostal tube is usually removed and the space is then collapsed by means of a thoracoplasty If no empyema is suspected and the parietal pleura and extraperiosteal tissue layer are intact, a paraffin plomb is inserted at the time of thoracoplasty[9, 10] However, when infection is suspected (or present), a conventional thoracoplasty of the Alexander type is utilized, performed usually in a single stage The latter is done also if the fascial and pleural partition is not intact Only rarely has a thoracoplasty been done with a drainage tube in place A secondary thoracotomy for closure of the leak or for a completion resection has been done infrequently in our group of patients

Prophylaxis is, of course, the best management, and in reviewing the problem one is able to make only a few basic conclusions Care in handling the bronchial stump, with adequate covering of the sutured stump with pleural or adjacent tissue whenever possible, is universally recognized as important Careful dissection in the intersegmental or interlobar plane with closure of any major leaks at the time of stripping is mandatory Preoperative or concomitant reduction of the size of the pleural space, although attractive, is not always feasible and prediction as to which patient is going to have a space problem is rarely possible Perhaps the use of preoperative bronchography in the patient with tuberculosis might aid in avoiding the inadvertent retention of, and possible injury to, an adjacent bronchiectatic segment during resection Even more fruitful might be the addition of a drug (corticosteroids) to the present antimicrobial therapy to reduce the amount of interstitial fibrosis seen in the treated tuberculous lung at the present time

SUMMARY

1 A review of 584 pulmonary resections (exclusive of pneumonectomy) for tuberculosis revealed an incidence of 128 (21 9 per cent) persistent pleural air spaces postoperatively

2 The incidence was highest following segmentectomy and lowest following a wedge resection

3 Of the persistent air spaces 86 (67 1 per cent) were asymptomatic and 42 (32 9 per cent) were symptomatic

4 The asymptomatic space was benign with respect to the patient's course whereas the symptomatic space proved hazardous and accounted for complications of varying severity in the 42 patients, with eventual death of 3

5. The greater the magnitude of the resectional procedure, the higher was the incidence of the symptomatic space.

6. Active treatment was not required in the asymptomatic space but multiple procedures were necessary to control the symptomatic space.

7. It is suggested that the peripheral air leak is the major offender in the etiology of the postoperative pleural air space and that the fibrosis now seen in the treated tuberculous lung may be a factor in its cause.

8. Early recognition and appropriate treatment of the patient with a symptomatic space will prevent more serious complications.

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DISCUSSION

DR JOHN W BELL, Seattle, Wash —I wish to compliment Dr Shields and his group for this very interesting study on the postresection space Certainly this continues to be an important problem Any complication which contributes to a mortality of 3 to 5 per cent is very significant

I think it should be emphasized that nearly three quarters of his cases were treated by conservative measures

We have been interested in this problem of postresection spaces for several years and, in general, our concept of the etiology of the space is similar to Dr Shields' in that if the residual lung is unable to fill the postresection space, such a problem will result

We have found that serial monometry is valuable in following some of these asymptomatic spaces We get rather jittery in determining whether a space will resolve or not, and by aspirating the space and determining the pressure at intervals it has helped us to determine whether or not a thoracoplasty or intubation is indicated

Most of the spaces which resolve spontaneously will maintain a neutral or negative pressure, whereas a space that shows positive pressure or reaccumulates fluid is probably a dangerous space, and it is usually the latter type that requires a postresection thoracoplasty

DR LAWRENCE H STRUG, New Orleans, La.—This problem has also plagued us in the deep South We have focused our attention on a prophylactic therapeutic procedure in attempting to eliminate the troublesome residual apical air space following lobectomy or lesser procedures

We have used preoperative pneumoperitoneum in a large number of selected cases on our combined services at Charity Hospital, and the Veterans Hospital of New Orleans, during the past 4 years We have been pleased with a marked decrease in the residual air space following the institution of this procedure Pneumoperitoneum is commenced approximately a week or 2 prior to surgery and continued for at least 6 to 8 weeks post operatively, and in the second and third categories as illustrated by Dr Shields it has been extremely helpful

It is obvious that when a major bronchial leak occurs, the space will become infected As a whole we have been extremely satisfied with this procedure and feel that it is an additional procedure which can be utilized to probably eliminate many problems of the residual apical air space

DR EDWARD F PARKER, Charleston, S C—We would like to mention one additional method of treatment which we have used with success and which we believe is clearly indicated in a few cases When there is an obvious disruption of the bronchial suture line manifested by fever, dyspnea—what one might call an internal open pneumothorax—and a cough with sputum consisting of fluid obviously coming from the pleural space, in such an instance we do not believe in trocar thoracotomy with closed drainage, but rather with open thoracotomy and re repair of the open bronchus We have had the misfortune of having to do this several times, but it is certainly the most effective method of treatment we have had so far

Second, when that is not done as a primary procedure, and trocar thoracotomy is done without closure of the fistula and without expansion of the lung, and therefore thoracoplasty becomes indicated, we believe that if there is only a one stage thoracoplasty necessary, the pleura should be opened at the same time and the bronchus closed surgically, rather than relying on the thoracoplasty alone to close it If there is more than one stage for the thoracoplasty necessary, we open the pleural cavity at the last stage to effect the closure of the bronchus, which we think is extremely important for permanent success

DR. JAMES E. DAILEY, Houston, Texas.—It might be mentioned that in order to facilitate the rapid obliteration of large residual pleural spaces and particularly when segmental or wedge resections are done, we have found it handy to initiate a pneumoperitoneum concomitant with the surgical procedure. In the East Texas Tuberculosis Hospital, Tyler, Texas, at the end of the operation and before closing the chest, we insert a small catheter directly through the diaphragm and with a large syringe and a three-way stopcock inject 1,000 to 2,000 c.c. of air into the abdominal cavity, thus elevating the diaphragm. The small incision is then closed by suture. Usually, no additional refills are necessary.

DR. SHIELDS (Closing).—I wish to thank Dr. Bell for his kind comments. We agree completely that the appearance of fluid in these spaces is an ominous sign and prompt institution of definitive therapy is indicated.

We did serial monometry early in our experience but have gotten away from it in the asymptomatic patient. Personally, I believe that the fewer needles put in these patients the fewer complications they are going to have.

In regard to pneumoperitoneum, we use it almost routinely; we are practically one of the few institutions in the country that use it extensively—preoperatively as well as postoperatively. If you recall the chest roentgenograms, it was present on most of the slides. Therefore, we don't indicate this as one of our major forms of therapy in this group of patients. If it is not present it is instituted early (during the first week) in any patient in which lung re-expansion appears to be slow and we don't want to wait for a 2-week period. We don't as a rule, however, induce it at the time of operation.

So far as direct repair of a bronchial stump fistula, we don't believe this is a good policy as a routine. I think that if the stump should break down early in the postoperative course, i.e., in the first several days, then re-exploration and primary repair might be indicated. However, one should look at the histologic slides to see whether or not tuberculosis endobronchitis is present, and, if it is, I think primary repair would be a very dangerous thing to do.

As to opening into the empyema space at the time of a thoracoplasty, this is very unappealing to us. In doing so you open up the subscapular space to infection.

Most of the overt bronchial pleural fistulas with empyema in our experience have been of the mixed variety and we have employed drainage and subsequent thoracoplasty for their control.

In closing, I wish to thank the discussers for their comments.

TRANSTHORACIC REPAIR OF ESOPHAGEAL HIATUS HERNIA: EVALUATION OF 200 CONSECUTIVE CASES

Lawrence K. Groves, M.D., William V. Martinez, M.D., and Donald B. Effler, M.D., Cleveland, Ohio*

HERNIATION of the stomach through the esophageal hiatus occurs frequently; in fact, the incidence of this diagnosis rivals that of inguinal hernia. The symptoms of esophageal hiatus hernia may be alleviated by medical treatment; however, as with other abdominal hernias, the basic problem is anatomic—the protrusion of abdominal contents through a defect in the abdominal wall—and definitive therapy entails surgical treatment.

In considering surgery for such a common condition, it is extremely important to know what risks are entailed, the probable effectiveness of the surgical treatment, and which patients with esophageal hiatus hernia should be advised to undergo surgery. This paper presents a study undertaken to answer these questions; it is based on our experience with 200 consecutive patients who were surgically treated for this lesion.

MATERIAL AND METHOD

For the purpose of evaluating selection of candidates and the respective postsurgical results, the charts were analyzed of 200 consecutive patients who underwent transthoracic repair of esophageal hiatus hernias in the 6 year period from 1951 through 1956. A large additional group of patients were operated upon, both before and since the time chosen for the survey, but this period was selected because (1) our surgical technique has undergone evolutionary improvement and in retrospect we are relatively unsatisfied with earlier operations, and (2) more recent cases had insufficient follow-up. This report is from a thoracic surgical service and includes only cases in which the operation was from this approach. Undoubtedly a satisfactory repair can be done through a laparotomy; however, in recent years the number of operations done from the abdominal approach at this institution has decreased steadily, probably indicating that surgeons have become relatively dissatisfied with it.

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TECHNICAL CONSIDERATIONS

It is our belief that the effective repair of a hiatus hernia involves more than mere reduction of the hernia and snugging-up of the hiatus about the terminal esophagus—a type of repair that is fraught with a high incidence of recurrent herniation. Many factors such as vomiting and straining in the post-anesthetic period may elevate intraabdominal pressure and force the stomach back up through even a very small hiatus. The placing of sutures from the margins of the hiatus into the friable esophageal musculature does not adequately protect against this hazard. Allison[1] has emphasized that the esophagogastric junction must be well fixed with sutures below the esophageal hiatus. His demonstration of the use of the phrenoesophageal ligament for this purpose was an important contribution, despite the many physicians who believe that this ligament is a rather nebulous structure.

In the repair that we have been using, the free peritoneal cavity is entered by circumferentially incising into it immediately above the esophageal hiatus across the peritonized portion of the thoracic stomach. The upper end of the hernial sac, consisting of parietal peritoneum as well as phrenoesophageal ligament, then retracts to form a cuff that nicely defines the esophagogastric junction and holds sutures firmly (Fig. 1). A ring of figure-of-eight sutures is placed deeply into this cuff and some of the underlying musculature (Fig. 2). These sutures are brought down through the hiatus and, through stab wounds made with a ligature carrier, out to the superior surface of the diaphragm where they are tied to mattress sutures placed about the stab wounds to fix the esophagogastric junction below the hiatus (Fig. 3). This maneuver probably is adequate for the average hernia; however, our standard procedure includes approximately the crura behind the esophagus with nonabsorbable suture material to form a snug ring (Fig. 4).

A rare patient has peptic esophagitis that has resulted in scarring and fixed esophageal shortening to such an extent that the esophagogastric junction cannot be reduced below the esophageal hiatus. This patient usually has severe symptoms. The controversy about the appropriate treatment of such patients indicates that no treatment is completely satisfactory. Our practice is to raise the esophageal hiatus to the esophagogastric junction by incising upward from the normal hiatus toward the dome of the diaphragm, and to transplant the esophagus forward to this new and elevated position (Fig. 5). In this fashion, considerable deficit in length can be overcome, particularly if the phrenic nerve is crushed to elevate the diaphragm maximally.[3]

Within the past year we have had our first experiences in having this technique not suffice to overcome the shortening. One patient underwent transplantation, but died of complications that were directly attributable to the excess tension used to accomplish the repair. Another patient was treated solely with digital dilatation of the terminal esophagus and a vagotomy. Thus far he has been essentially asymptomatic, and he has required only several office dilatations; no dietary restrictions or medication have been necessary. A gastric drainage operation has not yet proved necessary.

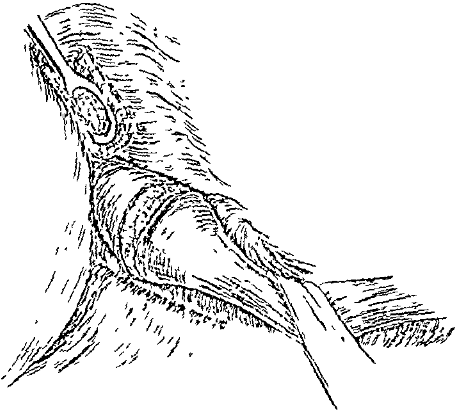
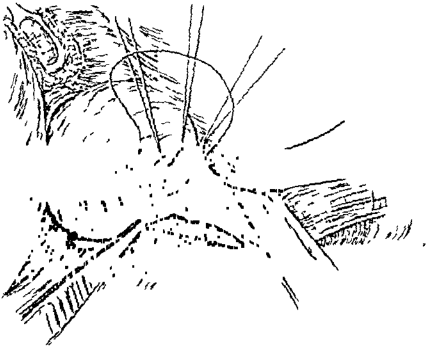


Fig. 1.—The terminal esophagus is being retracted by a rubber tape at the right; the diaphragm is being depressed by the sponge stick at the left. With the thoracic stomach thus exposed, the peritoneal sac is entered by circumferentially incising down onto the stomach a short distance above the diaphragm.



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Several of the patients who underwent the transplantation procedure each had large, scarified masses about the terminal esophagus, which scarcely could be distinguished grossly from neoplasm.

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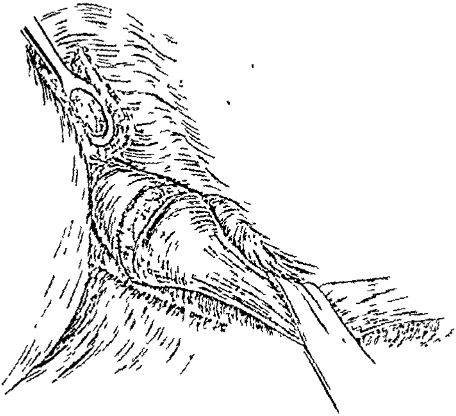

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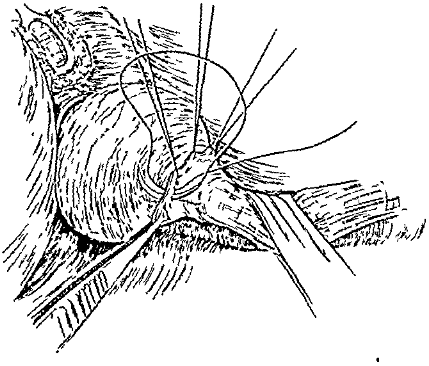

Fig 2—When the peritoneal sac is incised, as described in Fig 1 the upper cuff of the phrenoesophageal ligament and peritoneal sac nicely defines the esophagogastric junction A ring of figure-of-eight sutures is placed rather deeply into this cuff

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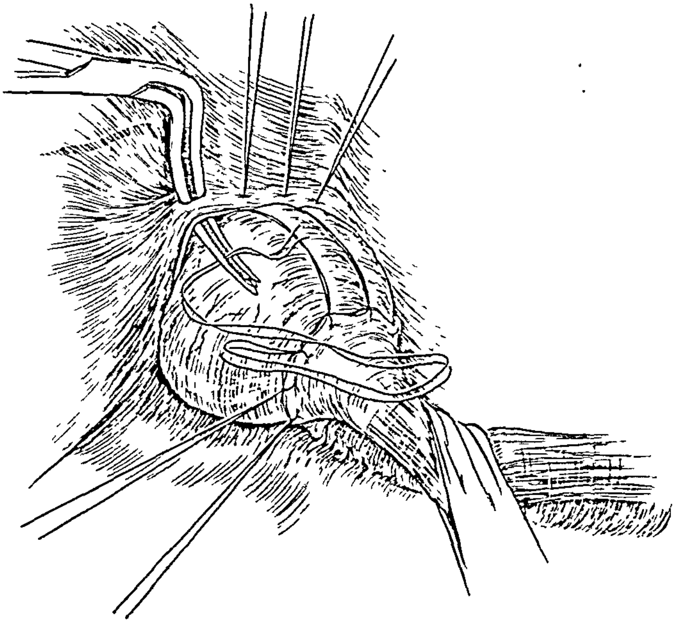


Fig. 3.—The ring of sutures is then brought down through the esophageal hiatus and through stab wounds made with a ligature carrier, out to the superior surface of the diaphragm. It is easy to visualize how traction upon this ring of sutures will then fix the esophagogastric junction below the esophageal hiatus.

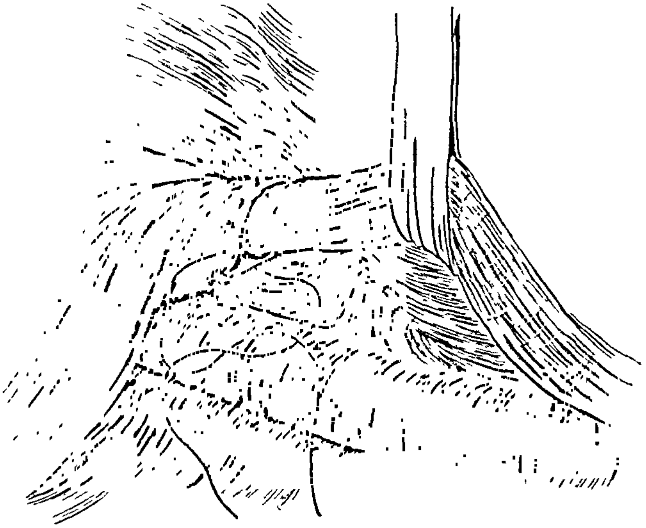


Fig. 4.—The previously placed ring of traction sutures has been tied to mattress sutures placed about the stab wounds in the diaphragm. The crura are then approximated behind the esophageal hiatus to give a snug closure.

continued use of this operative approach Certainly it seems reasonable to use such a conservative operation as a trial before resorting to an extensive resection or an interpositional procedure

METHOD OF FOLLOW UP

Identical questionnaires were sent to the 200 patients All of the patients were requested to return for examination if possible The questionnaire was worded so as to encourage frank answers For example, one question asked whether or not the patient considered his symptoms 100 per cent improved, and, if not, how much improvement there was, expressed in percentage Another question asked whether, if he had to decide again, he would or would not make the same choice, or whether he would have the operation sooner, or would try in every way to avoid operation The same questions were asked of the patients who returned for examinations, to maintain a uniform standard of evaluation A patient was considered lost to follow up if his records were not complete for at least 6 months after hospital discharge

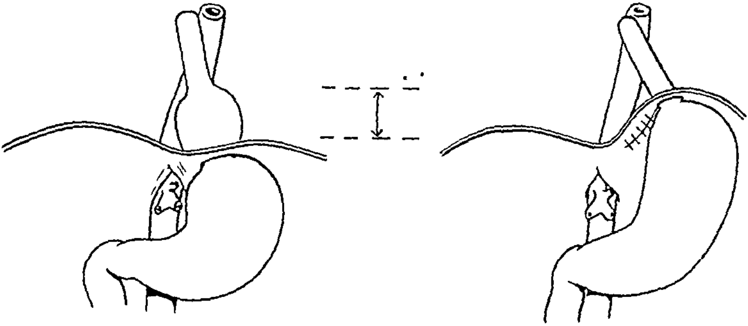
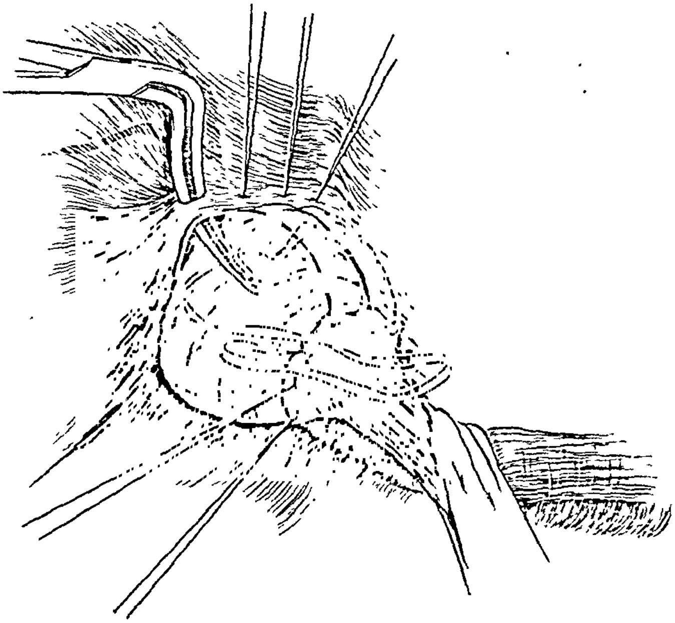


Fig 5—Crushing the phrenic nerve allows considerable elevation of the left hemidiaphragm This drawing demonstrates how esophageal shortening can be overcome by incising upward from the original hiatus toward the dome of the diaphragm The hernia repair is then performed by the method previously described

SELECTION OF PATIENTS

The data summarized in this paper refer only to patients who underwent surgical correction of hernias, asymptomatic patients were not operated upon For a large majority of patients who have esophageal hiatus hernias the surgical correction must be considered elective Usually, patients have distress of a peptic nature for many years without experiencing progressive severity, or complications related to the hernia It has been our policy to explain to such a patient the source of his symptoms, and that the operation should relieve them However, we also point out that the patient himself is the only one an operations have seemed to be rather drastic for a disease that is benign (benign histologically, but not clinically). We have been gratified to see patients who had advanced inflammatory changes become free of peptic symptoms after undergoing the conservative operation described above. Under these circumstances, postoperative dilation of residual strictures has given long-lasting relief from dysphagia. The results in 20 cases requiring transplantation, to us, justify



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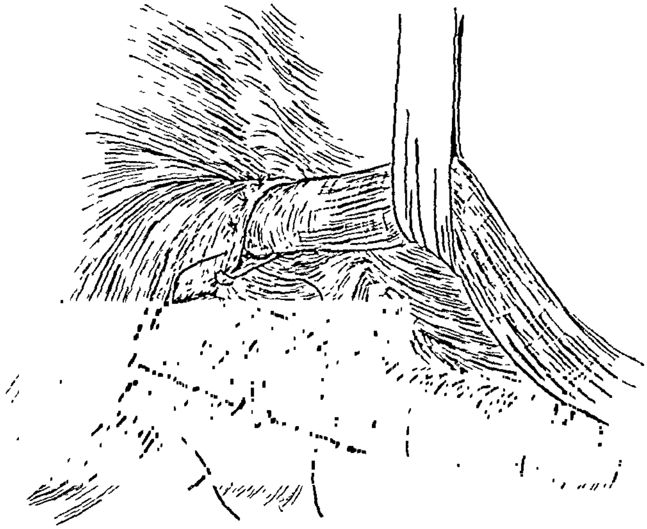

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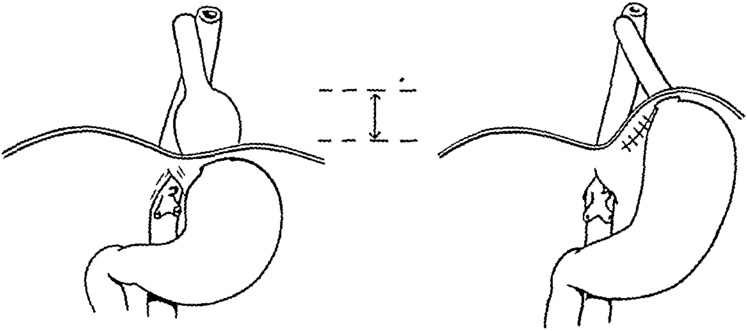

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The symptoms encountered in this series of patients are presented in Table I. A high proportion of the symptoms are of "peptic" origin. They are associated with the presence of acid gastric juice above the diaphragm. Heartburn is the most common symptom. Traditionally the peptic symptoms of hiatus hernia are blamed on reflux of gastric contents into the terminal esophagus. Except for the patient with short esophagus there is little objective evidence to support this concept. We have been impressed, both at surgery and by preoperative esophagoscopy, with the innocuous appearance of the esophageal mucosa in the majority of our patients. We have attempted to explain the mechanism of pain (or the absence of pain) in patients with uncomplicated hiatus hernia on the basis of gastritis within the thoracic stomach.[1] Its intensity may vary from mild distress to severe pain. The pain differs from that caused by a duodenal ulcer, in that it most frequently occurs shortly after eating, and the patient is apt to feel most comfortable when the stomach is empty. The pain often occurs at night, in the horizontal position, which is favorable to retention of gastric juice above the diaphragm.

TABLE I. SYMPTOMS IN 200 PATIENTS WITH ESOPHAGEAL HIATUS HERNIA

SYMPTOMS	NUMBER OF PATIENTS
Heartburn (post cibum; nocturnal)	145
Epigastric or substernal distress	138
Dysphagia	65
Regurgitation	55
Belching, flatulence, and bloating	35
Bleeding	35
Anorexia	29
Fullness	20
Indigestion	10

Spasm is one of the responses of the esophagus to irritation; hence dysphagia is a common symptom. However, dysphagia caused by spasm must be differentiated from that caused by contracture of scar tissue in the terminal esophagus. Usually, careful questioning of the patient as to the constancy of the difficulty in swallowing will make this differential. Most patients related that they sometimes could swallow normally, especially when they were relaxed, as on week ends or vacations, when gastric secretion presumably was minimal.

A lesser group of the symptoms is of mechanical origin. The most common of these is a feeling of fullness after meals, which doubtless is related to the distention of the thoracic stomach. Occasionally, and usually with large hernias, a volvulus at the level of the hiatus may cause a true mechanical obstruction, and may even jeopardize the supply of blood to the thoracic stomach.

A small group of patients had complications of esophageal hiatus hernia which made indications for surgery no longer elective and on occasion even emergent These complications are well understood and include (1) significant bleeding, (2) frank peptic ulceration, (3) stricture of the terminal esophagus, and (4) mechanical obstruction by volvulus[2]

Bleeding is a serious complication, in the series of 200 patients it was a chief indication for surgery in 35 (Table I) Frequently there is a history of isolated episodes of minor hematemesis or melena, but these 35 patients either had true massive loss of blood from the gastrointestinal tract and required transfusions, or had such a severe typical blood loss anemia that prolonged therapy either with iron or with transfusions or both was necessary as a preparation for surgery

Patients who have chronic anemia often have no typical symptoms of hiatus hernia, but they consult the physician for weakness or other nonspecific symptoms associated with anemia Under these circumstances, having demonstrated by the presence of occult blood in the stools a presumptive gastrointestinal origin of the bleeding, repair of the hernia is undertaken only after examination of the entire gastrointestinal tract has disclosed no other potential source of bleeding Only one patient with this type of bleeding has had bleeding since surgery Although it is our policy not to open and to explore the stomach during surgery unless a lesion is first palpable, we performed gastrotomy on several patients who had chronic bleeding, and the only notable abnormality was a hyperemic gastric mucosa which suggested that the loss of blood was due to a "weeping" gastritis

Massive bleeding, on the other hand, almost invariably comes from frank peptic ulceration in the thoracic stomach The usual site for these ulcers is either astride the esophagogastric junction, or at the level of the esophageal hiatus, as a callous ulcer, less frequently they occur at other sites in the thoracic stomach We believe that peptic ulceration within the thoracic stomach is related to the trapping of acid gastric juice therein, and that correction of the hernia and restoration of the normal gastric position and drainage should be curative It has not been necessary to operate on a patient while he was actively bleeding, and therefore we have not performed a gastric resection at the time of the hernial repair One peptic ulcer was excised locally for biopsy purposes This approach to the problem has proved effective in all except one patient He had recurrent bleeding and, inasmuch as the stomach was then in a normal position, gastric resection was performed in conventional manner

The age groups of the patients are summarized in Table II Hiatus hernia is clearly a disease of middle age Presumably the herniation is related to the loss of tone and the stretching of muscular and fascial structures associated with the aging process In this group of patients the incidence among the sexes has been about equal 103 women and 97 men

Although hiatus hernia is a common finding in obese adults, the majority of patients in this group were not obese Furthermore, it is our impression that reduction in weight has not been of great symptomatic benefit nor is it always easy to attain Fortunately, obesity is only a minor hindrance to thoracic surgery

TABLE II. AGE RANGE OF 200 PATIENTS WITH ESOPHAGEAL HIATUS HERNIA

AGE (YEARS)	NUMBER OF PATIENTS
20-29	3
30-39	9
40-49	53
50-59	61
60-69	66
70-79	7
80-89	1
Total	200

It is difficult to interpret the significance of the duration of symptoms as listed in Table III. It is obvious that a number of these patients have grown accustomed to their difficulties, and only chronic annoyance or gradual progression after a number of years has brought them to the physician. In others, the short history suggests recent onset of the hernia and the patient has promptly sought relief of symptoms.

TABLE III. DURATION OF SYMPTOMS IN 200 PATIENTS WITH ESOPHAGEAL HIATUS HERNIA

DURATION	NUMBER OF PATIENTS
<6 mo.	43
6-12 mo.	25
1-2 yr.	30
2-4 yr.	27
>4 yr.	75
Total	200

PREVIOUS SURGERY AND COLLATERAL PROBLEMS

The most common previous surgery in this group of patients was on the biliary tract (Table IV). It is difficult to evaluate the results of this surgery as it was performed at other institutions; however, the majority of those patients stated that cholecystectomy had not improved them, and their current symptoms were essentially unchanged from those noted preoperatively. This would suggest that though biliary tract disease and hiatus hernia frequently coexist, the surgeon should be careful of removing the gall bladder when there has not been typical colic and when the symptoms are the peptic type discussed previously. In this group of patients one might anticipate a high incidence of

TABLE IV. PREVIOUS SURGERY OR DILATATION IN SERIES OF 200 PATIENTS TREATED FOR ESOPHAGEAL HIATUS HERNIA

PROCEDURE	NUMBER OF PATIENTS
Biliary surgery	14
Dilatation	7
Abdominal repair of hiatus hernia	5
Thoracic repair of hiatus hernia	3
Vagotomy pyloroplasty	1
Heineke-Mikulicz operation	1
Phrenic crush	1
Multiple operations	1
Total	33

asymptomatic gall bladder disease, if it is carefully searched for Sixteen patients had abnormal cholecystograms whereas 61 had normal cholecystograms, 109 had no cholecystograms taken, the other 14 patients had had previous surgery upon the biliary tract

Eight patients had previous surgery for hiatus hernias, 5 through the abdominal and 3 through the transthoracic route At reoperation, save for evidences of adhesions and old suture material in the operative field, it was without exception impossible to distinguish these hernias from "virgin" cases

Seven patients had undergone previous dilatations It is our belief that if a patient with hiatus hernia needs dilatations, he should have a definitive surgical repair The stricture or spasm of the terminal esophagus is a response to the reflux of acid gastric juice Rational therapy would seem to entail reduction of the hernia, which will end this reflux, and thus remove the basic source of the dysphagia Unless this is done, a perpetual program of dilatation is apt to be necessary

The patient who required repair of a hernia following a Heineke Mikulicz esophagogastroplasty warrants a comment If this particular operation can be avoided at the esophagogastric junction it is our opinion that it should not be used Not only does it promote a mechanically incompetent esophagogastric sphincter and resultant esophagitis but also the shortening caused by the transverse closure of a vertical incision, of itself, tends to produce an esophageal hiatus hernia It has been our recent experience that, in those rare patients in whom technical considerations necessitate this type of reconstruction, if a careful effort is made to reduce the entire region of reconstruction, below the esophageal hiatus, the resultant pinching caused by passage of the esophagus through a snug hiatus and the associated angulation will preclude esophagitis due to regurgitation

The differential diagnosis of gall bladder disease and esophageal hiatus hernia already has been discussed A similar problem arises in differentiating between esophageal hiatus hernia and organic heart disease, particularly angina pectoris To take the history carefully is most important, the key points being the relation of distress to effort, as opposed to the occurrence of distress after eating and at night while at rest Certainly both conditions may produce types of distress that can be extremely difficult to distinguish from one another purely on the basis of a description of the symptom itself Electrocardiograms were performed on more than half of this series of patients and, of 108 tracings, abnormal changes were detected in 22 In 11 of the patients a diagnosis of angina pectoris was strongly suspected from the history

Once again it should be mentioned that this group of cases includes only those patients upon whom surgery was performed, in many other patients, although the same problems arose, surgery was not performed because of a suspected predominantly cardiac origin of the symptoms We believe that the decision involved in cases of concomitant angina pectoris and esophageal hiatus hernia is basically similar to the decision involved in cases of angina pectoris coexistent with disease of the biliary tract: if there are clear indications for surgery, it should be performed, with the recognition that the organic heart disease offers some element of increased risk. We have the distinct clinical impression that in this group of patients in whom one anticipates difficulty, one almost never actually encounters difficulty, presumbably because of the many added precautions that are taken. There was no mortality among the 11 patients. One has been lost to follow-up and the only failure occurred in a patient who was proved to have symptoms from only angina pectoris by complete failure of a technically satisfactory operation.

Rarely a patient who has a hiatus hernia may have episodes of sudden severe deep chest pains that resemble those in myocardial infarction. The mechanism is obscure, but the diagnosis usually becomes apparent when the expected electrocardiographic changes do not materialize.

TYPES OF OPERATION

The operations performed on these 200 patients are summarized in Table V. One hundred and sixty-three patients underwent a conventional repair, the technical points of which have been discussed. The additional procedures also are enumerated; some were performed consecutively through separate incisions during the one period of anesthesia. Two patients who each had an extremely large esophageal hiatus and rather attenuated muscle and fascia in the diaphragm had the hiatal repairs reinforced with stainless steel mesh; it was completely satisfactory.

TABLE V. SURGICAL TREATMENT IN SERIES OF 200 PATIENTS WITH ESOPHAGEAL HIATUS HERNIA

PROCEDURE	NUMBER OF PATIENTS
Routine (163)	
Reinforcement with wire mesh	2
Repair, epigastric hernia	2
Inversion, esophageal diverticulum	1
Excision, leiomyoma of esophagus	1
Excision, gastric diverticulum	1
Transcolonic polypectomy	1
Cholecystectomy	1
Repair, incisional hernia	1
Splenectomy	1
Routine and myotomy (17)	
Left lower lobectomy (for bronchiectasis)	1
Excision, juxtaesophageal ulcer	1
Transplantation (20)*	
Myotomy	7
Heineke-Mikulicz operation	1

*Gastric ulcer present in 6 patients.

In 17 patients who had an otherwise conventional repair and in 7 of the short-esophagus group who required transplantation, a myotomy was performed in the terminal esophagus. The indications for this procedure basically are that: (1) the patient has had considerable difficulty with dysphagia, and (2) at the time of operation the musculature of the terminal esophagus seems to be hypertrophic. This is a rather common operative finding, as is brought out by the frequency with which myotomy was performed. We consider it extremely important to ascertain by history whether or not the patient's dysphagia is intermittent or constant. Intermittent dysphagia proves that there is no organic narrowing of the terminal esophagus, and under these circumstances myotomy probably is superfluous. Also, we have often found it advantageous to assess digitally the lumen of the distal esophagus by making a small gastrotomy incision immediately adjacent to the cardia in the thoracic stomach. This is useful not only as a diagnostic maneuver but the finger is a sensitive and effective dilating instrument.

A word of caution should be said regarding myotomy in the presence of significant esophagitis. A myotomy may be exceedingly difficult to perform, as well as ineffectual, if there are inflammatory changes the full thickness of the esophageal wall. Under these circumstances the normal submucosal plane usually is obliterated and the lumen is easily entered unexpectedly. Furthermore, the muscularis may not gape upon reaching the submucosal plane, as with uninflamed tissue. We have found that making the myotomy incision down onto a finger (inserted through a gastrotomy) gives maximal control of the situation.

In 20 patients, or 10 per cent of the entire series, it proved necessary to transplant the esophageal hiatus in order to reduce the hernia. Although one can suspect preoperatively that this may prove necessary, a short esophagus cannot be diagnosed radiographically, and the true length and stretchability of the esophagus can be finally assessed only at the time of operation. In general, these are the most severely symptomatic patients with hiatus hernia, and have the greatest number of associated complicating factors; 6 of them had gastric ulcers in the thoracic stomach. It frequently is difficult to be sure whether such ulcers are in the esophagus or in the stomach, inasmuch as the stomach may be contracted and scarred and resemble the esophagus. Nevertheless, to date we have been unable to demonstrate other than gastric mucosa caudad to these ulcers, and believe that the esophagogastric junction always is above or at the level of the ulceration.

RESULTS OF SURGERY

The over-all results in the 180 patients who underwent surgical repair and were available for follow-up are summarized in Table VI; there were 161 conventional reparative operations, 19 transplantations. Results are classified as excellent, good, fair, failure. "Excellent" patients have total loss of gastric symptoms. A good result includes a subjectively pleased patient with only minor complaints. A fair result was reported in those individuals who believed the operation was worthwhile but who had significant residual problems, either gastric or incisional. The failures include all patients who were unimproved, became worse, or stated that they wished they had not had the operation performed, and the one operative death. Twenty patients have been lost to follow-up; they have not been seen or heard from more recently than 6 months after surgery. Table VII compares results as evaluated from the answers on the questionnaires, as against personal follow-up records for 55 patients who were seen more than 6 months after surgery, but who did not respond to the written follow-up program. The questionnaire results are more favorable than are the personal evaluations in the latter group of patients. This may be due to any of several factors, such as a more critical evaluation by the follow-up physicians than by the patients themselves, a tendency for the discontented patient to return with his problems, or, conversely, the feeling of the satisfied patient that there is no need to return.

TABLE VI. RESULTS IN 180 PATIENTS TREATED SURGICALLY FOR ESOPHAGEAL HIATUS HERNIA—FOLLOWED FOR FROM 6 MONTHS TO 6½ YEARS

RESULTS	NUMBER OF PATIENTS	PERCENTAGE OF 180 PATIENTS (%)
Excellent	97	53.9
Good	52	28.9
Fair	15	8.3
Failure	16	8.9
Totals	180	100.0

TABLE VII. FOLLOW-UP IN 180* PATIENTS TREATED SURGICALLY FOR ESOPHAGEAL HIATUS HERNIA: COMPARISON OF RESULTS REPORTED ON QUESTIONNAIRES AND FOUND ON EXAMINATION

SOURCE OF INFORMATION	NUMBER OF PATIENTS					PERCENTAGE OF PATIENTS† (%)			
	TOTAL	EXCELLENT	GOOD	FAIR	FAILURE	EXCELLENT	GOOD	FAIR	FAILURE
Questionnaire	125	77	33	7	8	61.6	26.4	5.6	6.4
Examination	55	20	19	8	8	36.4	34.6	14.5	14.5

*Twenty patients lost to follow-up.
†Questionnaire, based on total of 125 patients; examination, based on total of 55 patients.

In the group of 161 patients who underwent routine repair procedures, there were 13 results classified as failures (Table VIII). This group is discussed in more detail subsequently; another 13 patients were considered to have only fair results. These "fair" patients in most instances obtained satisfactory results as to their gastrointestinal symptoms, but were troubled with incisional problems.

TABLE VIII. RESULTS IN 180* PATIENTS OF TREATMENT FOR ESOPHAGEAL HIATUS HERNIA BY SURGICAL PROCEDURES—ROUTINE, MYOTOMY, OR TRANSPLANTATION

PATIENTS	ROUTINE, OR ROUTINE AND MYOTOMY†				TRANSPLANTATION‡			
	EXCELLENT	GOOD	FAIR	FAILURE	EXCELLENT	GOOD	FAIR	FAILURE
Number	89	46	13	13	8	6	2	3
Percentage (%)	55.2	28.6	8.1	8.1	42.1	31.6	10.5	15.8
	100				100			

*Twenty patients lost to follow-up.
†Based on 161 patients.
‡Based on 19 patients.

The results in patients with short esophagus that requires transplantation are gratifying, particularly in view of the fact that this is a highly symptomatic group of patients with many complications (Table VIII). Of 19 patients who were followed, only 3 considered their operations to have been failures. This seems to be a reasonable rate of failure for a conservative operation in a group of patients who have complicated conditions; moreover, further evaluation of these three failures is enlightening. One patient was addicted to Demerol and had other major psychiatric problems. Although the operation was definitely indicated, it is not surprising that she has obtained poor subjective results. The second patient states that he now swallows well and has dysphagia only on rare occasions; however, he maintains that his health is declining and that he is dissatisfied with the result. We have not evaluated this patient personally. The third patient has persistent, rather severe dysphagia and vomiting and undoubtedly represents a true failure.

Table IX summarizes the causes for operative failure in the 16 patients so classified. The major preventable cause of failure is poor selection of operative candidates. It is easy in retrospect to decide that a given patient should not have been operated upon. Esophageal hiatus hernias are such common findings in the course of a thorough evaluation of gastrointestinal symptoms that one may easily be misled into operating for what is basically a functional problem. It was appreciated that prior to surgery these patients had complicated organic and functional problems, and they were accepted for surgery only after they failed to respond to more conservative measures, and in several instances after psychiatric consultation.

TABLE IX. REASONS FOR 16 FAILURES AMONG 200 PATIENTS TREATED SURGICALLY FOR ESOPHAGEAL HIATUS HERNIA

REASON FOR FAILURE	NUMBER OF PATIENTS
Poor candidate for surgery	5
Persistent symptoms (heartburn, angina, bleeding, and dysphagia)	5
Neuralgia, anxiety tension state	2
Recurrent hernia (asymptomatic)	1
Gastric ulcer	1
Patient dissatisfied, health declining	1
Postoperative death (eighth postoperative day)	1
Total	16

The second group of 5 patients have persistence of their original symptom patterns, but no residual or recurrent hernias radiographically demonstrable. The patient who has persistent angina pectoris obviously had an incorrect interpretation of his symptom pattern prior to surgery. The patient who has persistent bleeding has had a subsequent laparotomy and resection of the colon for diverticulosis, but intermittent bleeding episodes of unknown source persist. Intercostal neuralgia after thoracotomy in 2 patients who had underlying anxiety tension states was sufficient to classify them as failures. One patient has definite radiographic evidence of recurrence, but is asymptomatic. One patient subsequently bled from a gastric ulcer and required gastric resection.

In this group of 200 patients there was only one operative death. This occurred on the eighth postoperative day and presumably was due to an acute myocardial infarction. Postmortem findings were equivocal. One patient in the transplantation group has already been mentioned as dissatisfied, and states that his health is declining, although he now swallows normally.

DISCUSSION

We have presented our technique for transthoracic repair of esophageal hiatal hernia and have tabulated the surgical indications and results in 200 patients. We also have attempted to weigh the importance of various factors in selecting patients for surgical correction. The results indicate that this surgery can be performed with low operative mortality, and a low incidence of recurrent hernia. In short, the operation is safe and mechanically effective, and should be done on the properly selected patient.

Patients with esophageal hiatus hernia symptomwise cover a broad spectrum. One end of this spectrum contains the asymptomatic patients, and is heavily populated. The other end contains the patients with severely symptomatic or the highly complicated hernias which have been discussed. Undoubtedly those patients in the severely symptomatic group, in the course of their disease, have traversed the entire length of the spectrum. However, it is only the exceptional patient whose hiatus hernia follows this progressive course. Thus, there is little justification in operating upon the asymptomatic patient. Furthermore, if symptoms should develop in such a patient they are almost invariably at first mild and it is safe to await the development of significant difficulties prior to electing surgery.

In between these two extremes lies a large group of symptomatic but uncomplicated cases. If these patients have increasingly severe symptoms, they should undergo surgery to relieve their symptoms and to avoid future complications. By far the largest group of symptomatic patients, however, has had relatively stable symptoms over a considerable period of time, and it is in this group that the greatest care in selecting surgical candidates must be exercised. One should be extremely careful of operating on patients who have other than the typical peptic type of symptom pattern. Careful roentgen study of patients who have functional gastrointestinal disease not infrequently will disclose an associated hiatus hernia; and, in retrospect, these patients constitute the largest group of dissatisfied patients. Operation in the "typical" patient must be considered elective. We feel it important to discuss the problem frankly with the patient and let him elect the operation rather than to "pressure" him into surgery. In the last analysis it is only the patient, himself, who knows how severe his symptoms are. One is thus able to exclude many patients who have symptoms that are subjectively only of "nuisance" value.

It is beyond the scope of this paper to discuss the physiology of symptoms in hiatus hernia. There are a number of factors concerned, important among which is the degree of gastric acidity. Others are volume of gastric secretion, pain threshold, tissue resistance, and consumption of gastric secretagogues.

It is difficult to distinguish physiologically between symptomatic and asymptomatic hiatus hernias. Probably few asymptomatic patients have hypersecretion of gastric acid; conversely, it is distinctly unusual for the patient whose severely symptomatic hernia is successfully repaired to experience further difficulty from gastric hyperacidity (i.e., duodenal ulcer). Nevertheless, it probably is fair to state that a roughly linear relationship exists between gastric acidity and severity of symptoms and incidence of complications. This is the rationale for treating hiatus hernia by gastric resection, vagotomy, and/or gastric drainage procedures. However, we believe that the results summarized here indicate that the degree of acidity may be largely ignored and that an "anatomic" operation is usually preferable to a "physiologic" one.

Mention should be made of the fact that the physical size of the esophageal hiatus hernia has little or no bearing upon the severity of symptomatology and, hence, upon the selection of patients for surgery. It is only the very large hernia that can develop volvulus and mechanical obstruction but as far as the peptic symptoms are concerned, the presence of a hiatus hernia of any size creates the proper anatomic conditions for regurgitation of acid gastric juice. Several of the excellent results in this series occurred among patients whose roentgenograms showed no definite evidence of an esophageal hiatus hernia, and in whom, at the time of surgery, one could argue as to whether or not there was a true hernia or merely a relaxation of the esophageal hiatus and phreno-esophageal ligaments. However, in these patients mild traction on the esophagus will definitely pull the esophagogastric junction above the level of the esophageal hiatus.

We have used a myotomy in the terminal esophagus quite frequently and believe this to be a useful adjunct in those patients with dysphagia. It does, however, have definite limitations, particularly in the presence of significant inflammatory changes in the esophageal wall, and it is not likely to be of much benefit in a truly fibrotic stricture, the significant portion of which is apt to be mucosal or submucosal in location.

In those complicated cases with true organic shortening of the esophagus, if at all possible, we have tried to avoid esophagogastric resection. Admittedly, the deformed and scarred cardia has lost the ability to function physiologically; however, we believe that the results in 20 patients who were treated by conservative transplantation operations with or without myotomy and subsequent dilation endorses this approach to the problem.

SUMMARY AND CONCLUSIONS

Surgical experience and follow-up of 200 consecutive operative cases of esophageal hiatus hernia are reviewed. The operation as described has given highly satisfactory results in regard to postoperative recurrence and operative mortality. Operation is mandatory in a small proportion of patients who have complications, including bleeding, peptic ulceration, stricture of the terminal esophagus, mechanical obstruction. In the large majority of patients, the operation is elective. These patients will obtain excellent operative results if they are carefully selected for surgery. In retrospect, the largest number of preventable operative failures has been classified as being due to a poor choice of operative candidates, including chiefly emotionally unstable patients and those whose gastrointestinal problems are largely functional.

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SINGLE DOSAGE X-RAY RADIATION TO THE LUNG AND POSTERIOR MEDIASTINUM THROUGH THE OPEN CHEST

II. Results in Animals Receiving a Dose of 5,000 r

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CLIFFTON, Henschke, and Selby[2] and others have had experience with interstitial implantation of neoplasms at the time of thoracotomy Chesney and Daughtry[1] have radiated the lung through the open chest at the time of exploration for bronchogenic carcinoma Because of the limited experience with the latter method, a laboratory study was undertaken The results in animals receiving doses between 6,000 r and 15,000 r have been published[4] A second series of dogs receiving doses of 5,000 r has now been observed

MATERIALS AND METHODS

The method of study was essentially as previously described,[4] and is summarized in Fig 1. The dogs were divided into three groups Groups I and III received the radiation directly to the expanded right lung but the radiated area was much larger in Group III. Those animals in Group II received the radiation to the posterior mediastinum with protection of the parenchyma of the right lung The field in this group closely approximated that of Group I

RESULTS

The autopsy findings and survival times on the dogs are summarized in Table I Almost all of the animals died as a direct result of the radiation administered When there was necrosis of the trachea, the process often involved the lung with erosion of one of the pulmonary vessels In these instances, the animals sustained a fatal hemoptysis Usually when the esophagus was perforated there was not a free communication into the pleural space but penetration into the posterior mediastinum Fig 2 demonstrates the esophagus in a dog that developed a tracheoesophageal fistula Fig 3 shows the trachea in another dog that died as a result of a tracheoesophageal fistula Dog X-35 bled to death as a result of an aortic esophageal fistula and also had an area of necrosis in the trachea (Fig 4)

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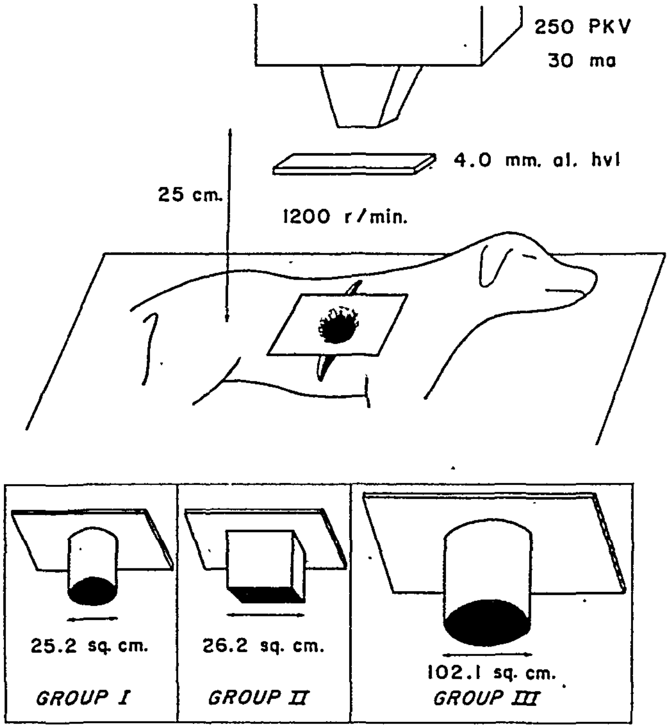

Fig. 1.—The various x-ray factors are shown diagrammatically. Those dogs in Group I received radiation directly to the expanded lung through a portal of 25.2 sq. cm. The surrounding tissue was protected, as shown in the inserts, by at least 2 mm. of lead. The dogs in Group III were similarly treated but the portal was 102.1 sq. cm. In Group II a rectangular portal of 26.2 sq. cm. allowed radiation of the posterior mediastinum but protected the lung. All operations were performed under general anesthesia using sterile technique.

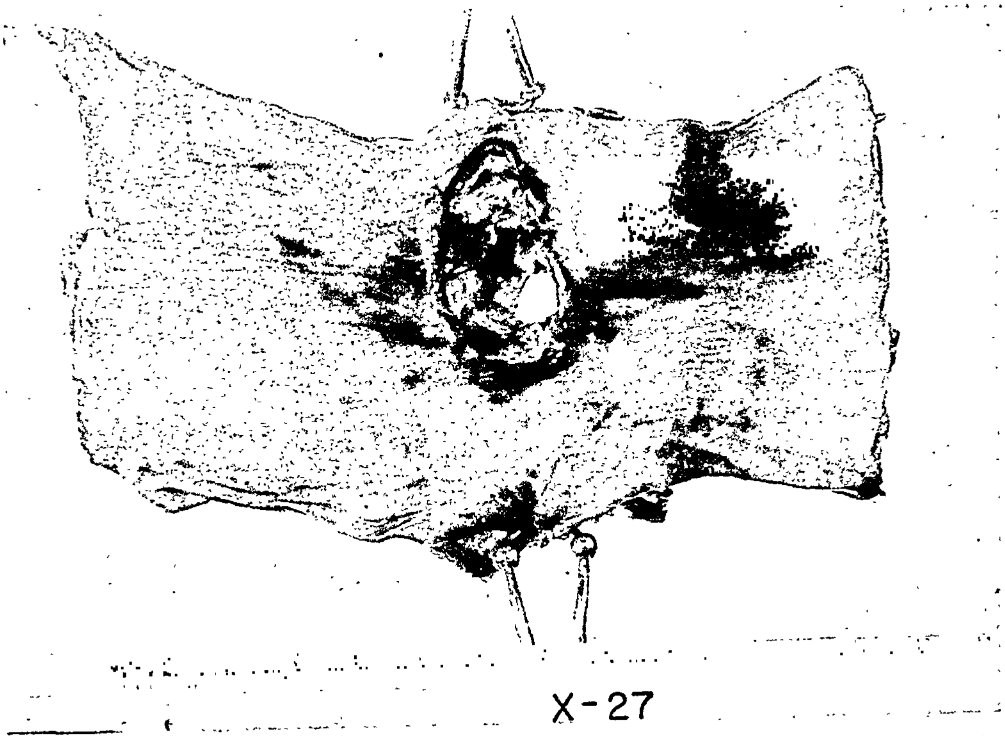

Fig. 2.—This dog of Group I lived 232 days following radiation. He appeared to be in good health, without weight loss or change in blood count until 48 hours before death. The photograph shows the esophageal side of a tracheoesophageal fistula. There was considerable fibrosis of the radiated lung and posterior mediastinum in addition to the acute pneumonia.

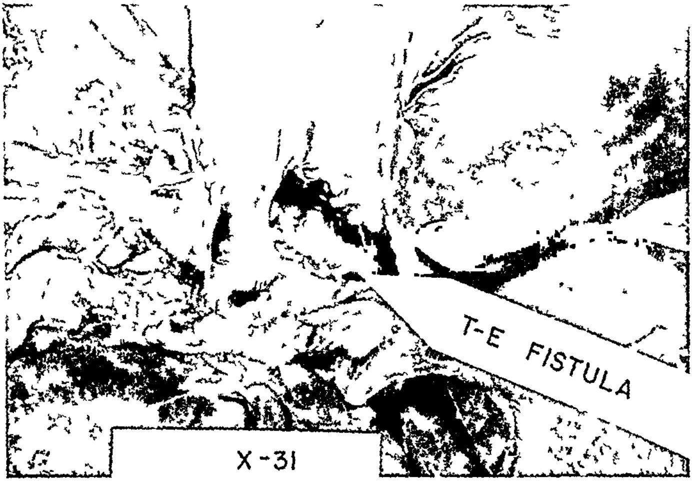

Fig 3—The trachea from another dog from Group I that developed a tracheoesophageal fistula is shown The tracheas of the animals that developed necrosis of the trachea without fistula presented appearances similar to this

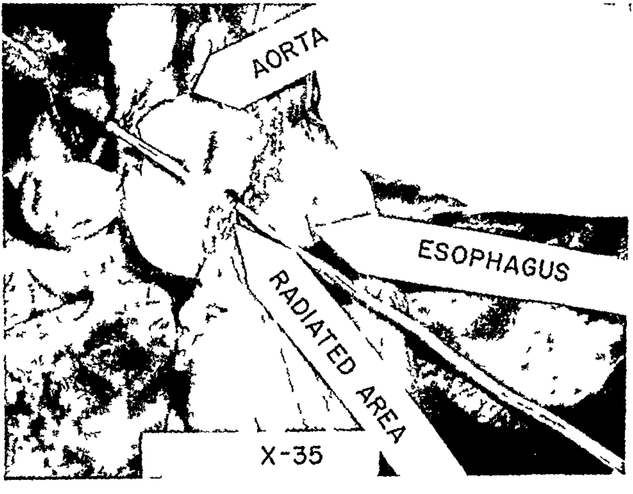

Fig 4—This dog from Group II bled to death as the result of an aortic esophageal fistula There was also an area of necrosis of the trachea.

The animals did not show a constant change in hemoglobin determinations or in white blood cell counts. The operations were well tolerated and almost all animals exhibited no difficulty until 24 to 48 hours before death.

The survival times of the dogs in the three groups were plotted (Fig. 5). Significant statistical difference existed only between Groups I and III.* It was therefore postulated that the area radiated in relation to the size of the animal was a determining factor in survival time. Using the formula developed by Meek and Rubner,[3] the surface areas of the dogs were compared to the survival times but no relationship could be demonstrated.

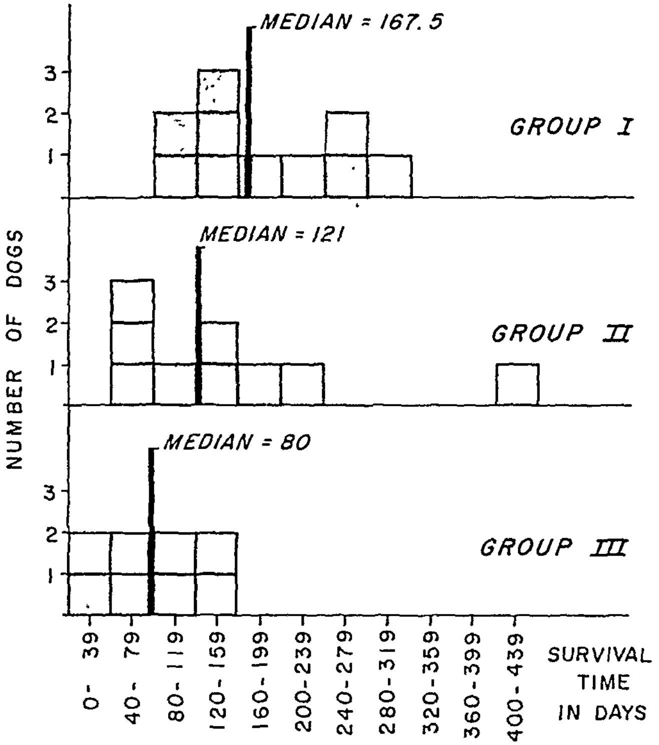

Fig. 5.—The number of dogs in each group are plotted against the survival times. Each square represents one dog. Statistically a significant difference (P 0.01) in survival times existed only between Groups I and III.

DISCUSSION

Chesney hoped that the administration of single dose x-ray radiation through the open chest to the lung of patients with bronchogenic carcinoma would materially decrease the morbidity associated with palliative radiation given by conventional methods. The morbidity was apparently much reduced since, as has been stated, the animals did well until shortly before death. Undeniably this method of radiation would be useful if it allowed a larger or more effective tumor dose than can be delivered by radiation through the chest wall. It was obvious that 5,000 r was a much larger than cancerocidal dose and resulted in almost 100 per cent mortality. It was also obvious that 5,000 r

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*The Wilcoxon-White Two-sample Rank Test was used to test the significance of the difference between the medians of the groups.

TABLE I

DOG	WEIGHT (KG)	SURVIVAL IN DAYS	AUTOPSY FINDINGS
Group I			
X 27	26 3	232	T* E* fistula
X 28	30 8	282	Necrosis of T
X 29	27 4	179	Mediastinal fibrosis Pneumonitis
X 30	14 0	156	Periesophagitis Pneumonitis
X 31	13 6	87	T E fistula
X 32	14 0	92	Necrosis E L*
X 54	13 6	138	Necrosis T E
X 55	15 9	140	Necrosis T E Bilateral pneumonitis
X 56	15 9	262	Perforation of E
X 57	15 3	257	Ulcer E Fibrosis of L
Group II			
X 34	6 8	114	T E fistula
X 35	7 0	209	Necrosis T E T A* fistula
X 36	9 5	42	Empyema
X 37	—	73	Perforation of E Necrosis T
X 50	8 9	55	Ulcer of E
X 51	15 9	167	Ulcer of T E A E fistula
X 52	13 6	142	T E fistula
X 53	15 4	121	Perforation of E Empyema
X 49	10 4	411 living	—
Group III			
X 39	15 9	143	Perforation of E Necrosis of T
X 41	13 6	82	Necrosis of T Mediastinal fibrosis Necrosis of L
X 42	13 8	104	Mediastinal fibrosis Lung necrosis
X 43	15 9	19	Empyema Fibrosis of L
X 45	11 8	23	Wound infection
X 46	11 4	78	Tracheitis Pneumonitis
X 47	9 0	146	Bronchopleural fistula Necrosis of L Esophagitis
X 48	29 5	46	Pneumonitis

*T = trachea E = esophagus L = lung A = aorta

administered as a single dose could not be compared to 5,000 r given in small increments over a period of weeks Although the animals died as the result of the radiation, the autopsy findings were considerably different from those in the series receiving the higher doses [3]

The factor or factors that accounted for the significantly longer survival time in the animals in Group I, as compared with Group III where the field was over four times larger, remained obscure It was speculated that the surface area radiated in relation to the surface area of the dog accounted for this Critical analysis of the data, however, did not confirm this theory

The animals did not show a constant change in hemoglobin determinations or in white blood cell counts. The operations were well tolerated and almost all animals exhibited no difficulty until 24 to 48 hours before death.

The survival times of the dogs in the three groups were plotted (Fig. 5). Significant statistical difference existed only between Groups I and III.* It was therefore postulated that the area radiated in relation to the size of the animal was a determining factor in survival time. Using the formula developed by Meek and Rubner,[3] the surface areas of the dogs were compared to the survival times but no relationship could be demonstrated.

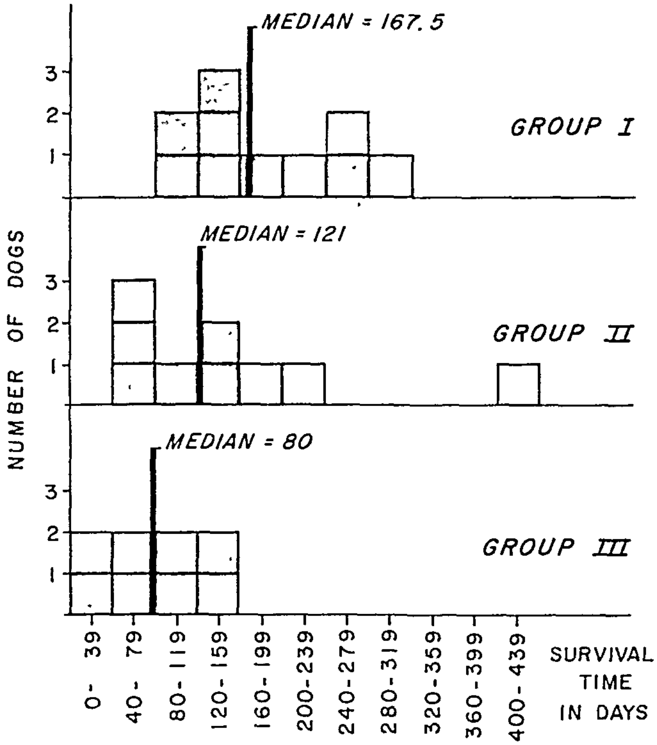

Fig. 5.—The number of dogs in each group are plotted against the survival times. Each square represents one dog. Statistically a significant difference (P 0.01) in survival times existed only between Groups I and III.

DISCUSSION

Chesney hoped that the administration of single dose x-ray radiation through the open chest to the lung of patients with bronchogenic carcinoma would materially decrease the morbidity associated with palliative radiation given by conventional methods. The morbidity was apparently much reduced since, as has been stated, the animals did well until shortly before death. Undeniably this method of radiation would be useful if it allowed a larger or more effective tumor dose than can be delivered by radiation through the chest wall. It was obvious that 5,000 r was a much larger than cancerocidal dose and resulted in almost 100 per cent mortality. It was also obvious that 5,000 r

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*The Wilcoxon-White Two-sample Rank Test was used to test the significance of the difference between the medians of the groups.

TABLE I

DOG	WEIGHT (KG)	SURVIVAL IN DAYS	AUTOPSY FINDINGS
Group I			
X 27	26.3	232	T*-E* fistula
X 28	30.8	282	Necrosis of T
X 29	27.4	179	Mediastinal fibrosis Pneumonitis
X 30	14.0	156	Periesophagitis Pneumonitis
X 31	13.6	87	T E fistula
X 32	14.0	92	Necrosis E L*
X 54	13.6	138	Necrosis T E
X 55	15.9	140	Necrosis T E Bilateral pneumonitis
X 56	15.0	262	Perforation of E
X 57	15.3	257	Ulcer E Fibrosis of L
Group II			
X 34	6.8	114	T E fistula
X 35	7.0	209	Necrosis T E T A* fistula
X 36	9.5	42	Empyema
X 37	—	73	Perforation of E Necrosis T
X 50	8.9	55	Ulcer of E
X 51	15.9	167	Ulcer of T E A E fistula
X 52	13.6	142	E T fistula
X 53	15.4	121	Perforation of E Empyema
X 49	10.4	411 living	—
Group III			
X 39	15.9	113	*Perforation of E* *Necrosis of T*
X 41	13.6	82	*[illegible] of T* *Mediastinal fibrosis* *Necrosis of L*
X 42	13.8	104	*Mediastinal fibrosis* *Lung necrosis*
X 43	15.9	19	*Empyema* *Fibrosis of L*
X 45	11.8	23	*Wound infection*
X 46	11.4	78	*Tracheitis* *Pneumonitis*
X 47	9.0	146	*Bronchopleural fistula* *Necrosis of L* *Esophagitis*
X 48	9.5	16	*Pneumonitis*

*T = trachea E = esophagus, L = lung A = aorta

administered as a single dose could not be compared to 5,000 r given in small increments over a period of weeks Although the animals died as the result of the radiation the autopsy findings were considerably different from those in the series receiving the higher doses[3]

The factor or factors that accounted for the significantly longer survival time in the animals in Group I, as compared with Group III where the field was over four times larger, remained obscure It was speculated that the surface area radiated in relation to the surface area of the dog accounted Critical analysis of the data, however, did not con

Additional work must be done to determine the maximum safe dose of radiation that can be delivered by this method. Assuming that this dose is cancerocidal, it will have to be determined how much physiologic change occurs as a result of the radiation. Thus, considerable decrease in pulmonary function or late pulmonary hypertension might make the procedure useless.

SUMMARY

1. Thoracotomies were done on dogs. Group I received 5,000 r through a portal of 25.2 sq. cm. directly to the lung. Group III were treated similarly but the field was 102.1 sq. cm. Group II received the radiation to the posterior mediastinum only, with the lung protected.

2. Almost all animals died as a direct result of the radiation administered. Group I dogs survived significantly longer than Group III. No relationship between surface area of the dog and area radiated could be demonstrated.

3. Additional work must be done to establish the safe maximum dose of x-ray that can be tolerated by this method.

The assistance of Dr. John B. Miale and Miss Iris Kiem is gratefully acknowledged.

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Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Fortieth Annual Meeting of The American Association for Thoracic Surgery will be held May 11, 12, and 13, 1960, in Miami Beach, Florida. Headquarters will be the Deauville Hotel.

Requests for Hotel Reservations

These should be mailed directly to Mrs. Mildred Sander, Reservation Manager, Deauville Hotel, Miami Beach, Florida. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere please communicate directly with the hotel of your choice.

Material for the Program

SCIENTIFIC PAPERS.—Abstracts of all papers proposed for presentation at the 1960 meeting *must be received on or before* **November 15, 1959,** otherwise they will not be considered by the Program Committee. These should be labeled "For Thoracic Surgery Forum" or "For Regular Program" depending upon the nature of the subject matter, in the same manner as in previous years. They should contain from 200 to 250 words that accurately reflect the content of the completed paper.

Six, repeat, six clearly legible copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, 308 Carondelet Building, 7730 Carondelet Avenue, St. Louis 5, Missouri.

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary *immediately* after their presentation If they are not ready at that time there is a chance that they will not be published in THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than* **November 15, 1959,** otherwise the application will be deferred for consideration until the 1961 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Frank Gerbode, M.D.
Chairman of the Membership Committee
Stanford University Hospital
San Francisco 15, California

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applicants be held over for reconsideration a *second year.*

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Original Communications

METABOLIC ACIDOSIS AND THE DISSOCIATION CURVE OF HEMOGLOBIN DURING EXTRACORPOREAL CIRCULATION

George J. Magovern, M.D. (by invitation), Robert S. Cartwright, M.D. (by invitation), John F. Neville, Jr., M.D.** (by invitation), and Edward M. Kent, M.D., Pittsburgh, Pa.*

THE PHYSIOLOGIC value of hemoglobin as an oxygen carrier lies in the fact that its affinity for oxygen is so balanced that, in the lungs, hemoglobin becomes 95 to 96 per cent oxygenated, while in the tissues and the capillaries it can give up as much of the oxygen as demanded. The relationship between oxygen tension and the degree of saturation of hemoglobin has been studied in blood and in solutions of hemoglobin by Huffner, Bohr, and others. The effect of alkalinity was first noted by Bohr, Hasselbalch, and Krogh[1] who observed that increasing carbon dioxide tension decreased the amount of oxygen bound by hemoglobin. Barcroft[2, 3] showed that the degree of oxygenation, although dependent chiefly on the oxygen pressure, also increased with the alkalinity and the electrolyte content of the blood. They subsequently showed that the effect of carbon dioxide was due to its acidity and that the addition of other acids to the blood had a similar influence. Fig. 1 depicts the S-shaped curve of oxyhemoglobin dissociation and shows the relationship between oxygen tension, oxygen saturation, and varying pH. It will be noted that, as the blood becomes more acid, hemoglobin combines with less oxygen and, as the blood becomes more

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Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

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alkaline, the opposite is noted. Conversely, the amount of oxygen which is released to the tissues is greater at a reduced pH than it is at an alkaline pH. It is this behavior which enables oxygen to dissociate from the blood as it reaches the tissues, taking up in its place carbon dioxide. The changes in oxyhemoglobin dissociation effected by changes in the pH is known as the Bohr effect.

The purpose of this study was to determine to what advantage this physiologic reaction may be applied during extracorporeal circulation. It was based on clinical observations in our own series of approximately 100 open-heart operations. In 12 instances when the arterial pH was reduced, we believed a clinical improvement and a gross color change were brought about by the addition of sodium bicarbonate to the blood during bypass.

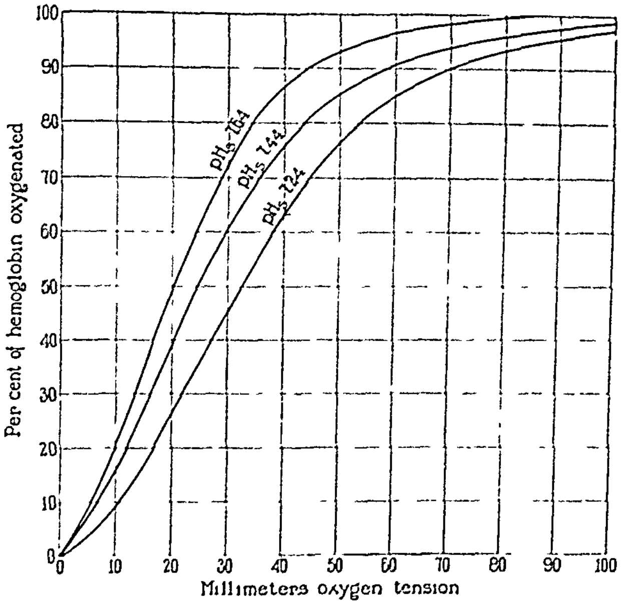

Fig. 1.—Relationship between oxygen tension and oxygen saturation of human blood at varying pH. Curves calculated by Richards and Strauss (Ref. 11).

METHOD

A. *Experimental Procedure.*—Twenty-five dogs were anesthetized with Pentothal sodium, 30 mg. per kilogram of body weight. Utilizing a multiple disk Kay-Cross oxygenator and 95 per cent oxygen and 5 per cent carbon dioxide, the animals were placed on total cardiopulmonary bypass. This was done through a right thoracotomy which was performed under aseptic technique. Venous drainage was enacted into the oxygenator by gravity after catheters were placed in the superior and inferior vena cava via the right atrial appendage. The arterial return was through the right femoral artery. The left femoral artery was cannulated with a No. 190 polyethylene catheter for continuous monitoring of the arterial pressure. This catheter was threaded into the central aorta and the pressure was determined with an aneroid manometer. A similar catheter was placed into the inferior vena cava through the saphenous vein and connected to a saline manometer for continuous monitoring of the venous pressure After tapes were placed around the superior and inferior vena cava, the catheters were inserted and total cardiopulmonary bypass was begun The animals were perfused according to the amount of venous return, maintaining a venous pressure of 0 to 1 cm of water The animals varied in weight from 12 to 22 5 Kg and were perfused at flow rates of 26 to 87 c c per kilogram a minute After complete bypass was initiated and satisfactory flow and oxygenation were achieved, hypoxia was produced by reducing the revolutions of the disks from 120 to approximately 60 r p m This caused inadequate surface area exposure, resulting in reduction of the partial pressure of oxygen and undersaturation of the blood Particular emphasis was placed on the avoidance of changes in the blood level in the oxygenator and flow rates once the experiment was begun With the development of hypoxia, monitoring of the pH was carried out and, as acidosis occurred due to the anoxia, the pH was noted to fall

At a reduced pH, which averaged approximately 7 25, samples of blood at the venous inlet and the arterial outlet of the oxygenator were taken for measurement of oxygen and carbon dioxide content The pH at the arterial end of the oxygenator was simultaneously recorded at this time Correction of the reduced pH was then attempted by the addition of alkali or the creation of respiratory alkalosis The alkali added was either sodium bicarbonate, 44 6 mEq per 50 c c of solution or 1 M sodium-r lactate, 1 mEq per cubic centimeter of solution The production of respiratory alkalosis was achieved by changing the gas mixture from 95 per cent oxygen and 5 per cent carbon dioxide to 100 per cent oxygen, thereby allowing carbon dioxide to escape from the blood

B *Analytical Methods*—The following determinations were performed on the blood samples (1) plasma pH, (2) total carbon dioxide content, and (3) total oxygen content

Total oxygen capacity was determined from a sample taken from the oxygenator at the completion of the experiment so that complete mixing of the patient and donor blood was achieved, thereby giving an over all hematocrit Two of the experiments were analyzed for sodium, potassium, chloride The pH determinations were done on whole blood at a constant temperature of 36° C in a Beckman model G pH meter, accuracy plus or minus 0 05 pH units Total carbon dioxide, total oxygen content, and oxygen capacity were determined according to the method of Van Slyke and Neill[4] Sodium and potassium determinations were carried out on a Coleman flame photometer Chloride was determined according to the method of Sendroy and his associates[5]

C *Calculations*—The pCO_2* and base bicarbonate were calculated from the measured pH and the total plasma carbon dioxide using the Henderson Hasselbalch equation with pK′ equal to 6 10 The plasma carbon dioxide was calculated from the whole blood carbon dioxide content[6] The per cent of oxygen saturation was calculated by dividing the total oxygen content by the total oxygen capacity and multiplying by 100 The oxygen tension of the blood was determined from the pH and arterial saturation

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*Partial pressure of carbon dioxide expressed in millimeters of mercury

EXPERIMENTAL OBSERVATIONS ON POST-STENOTIC DILATATION

David L. Bruns, M.D. (by invitation), John E. Connolly, M.D. (by invitation), Emile Holman, M.D., and Raymond C. Stofer, D.V.M. (by invitation), San Francisco, Calif.

A most puzzling phenomenon encountered in medicine is the dilatation of a vessel downstream from a stenosis. Though not universally found, it is sufficiently common to be looked for when aortic or pulmonic stenosis, or coarctation of the aorta is being considered (Fig. 1). A striking feature is that post-stenotic dilatation may occur in a region where a relatively low pressure exists.

In cases associated with congenital defects, an accompanying weakness of the adjacent vessel wall might lead to dilatation. However, its failure to develop in a high pressure region upstream, in the case of coarctation, is difficult to explain without assuming that the weakness of the congenital vessel wall is peculiarly restricted to the downstream region. Futhermore, it is seen with acquired valvular stenosis, which does not strengthen this hypothesis. Last, it can be produced easily in the healthy vessel walls of experimental animals.[1, 2]

Our original interest lay not in the cause of post-stenotic dilatation, but in the cause of murmurs. This led to a better understanding of the fluid mechanics of blood flow, and this knowledge has been applied to post-stenotic dilatation.

By reviewing the factors involved in the production of murmurs, it was found that the classic theory that murmurs are due to turbulence is an unreasonable one. A new theory was proposed which attributed murmurs to nearly periodic pressure fluctuations in the wake downstream from an obstacle or constriction.[3] These fluctuations develop in response to the shedding of vortices and are of a magnitude large enough to produce audible sound. The basic mechanism is that found in the production of Aeolian tones. Because of the lack of symmetry and smoothness around or through which blood must pass, the pressure fluctuations are not strictly periodic. As a result, noise rather than a clear tone is produced. However, the same order of acoustical efficiency is realized. The discrete pressure fluctuations are of an intensity much greater than those one would expect from turbulence.[4] As such, they are better generators of noise.

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Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

One of the characteristics of periodic or nearly periodic wakes is that most of the energy which this type of flow produces is concentrated in the region immediately downstream from the obstacle or constriction; and, thus, one would expect murmurs to be most intense in this region. This expectation is realized both in experimentally induced stenosis as well as in one's ability to localize murmurs clinically. If this is true for murmurs so also must it be true for thrills, and one would expect the vessel wall vibrations of a thrill to be maximal in intensity a short distance distal to the stenosis. It was then postulated that the damage resulting from these local vibrations may so affect the vessel wall that structural fatigue would ensue. If so, this could lead to dilatation even in a region of low pressure. Our experiments were designed to test this hypothesis (Fig. 2).

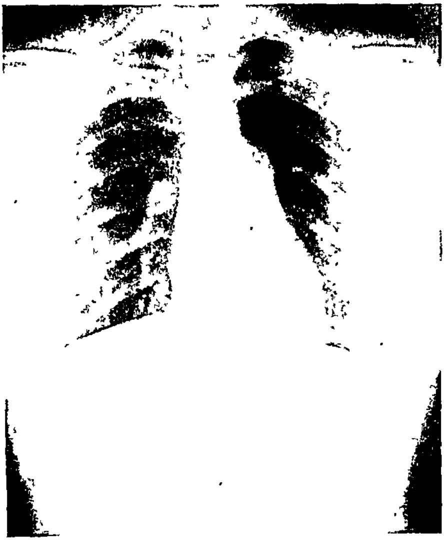

Fig 1.—Preoperative chest x-ray film of a 10-year-old girl with congenital valvular pulmonic stenosis and considerable dilatation of the pulmonary artery segment. Right ventricular and pulmonary artery pressures were 141/8 and 14 (mean) mm Hg Fifteen months postoperatively the right ventricular pressure had fallen to 40/4 mm. Hg and the mean pulmonary artery pressure remained the same. There was no change in the chest x-ray film. (Patient of Drs R Gross, H Hultgren, F Eldridge, and F. Gerbode)

METHODS AND RESULTS

It was desirable to use elastic tubes so as to approximate the structure of vessel walls in which post-stenotic dilatation is encountered. These tubes should be thin-walled so that any structural fatigue will be manifested in a relatively brief period of time. The latex rubber tubing used as Penrose drains served admirably.

These tubes were filled with water and a static pressure was maintained. They were plugged with rubber stoppers at both ends so that no flow could take place. Through one of the stoppers a vibrating blade was inserted. This was driven by a pipette shaker (Fig. 3). The amplitude of the oscillations was maximal at the tip of the blade. The vibrating rate was determined

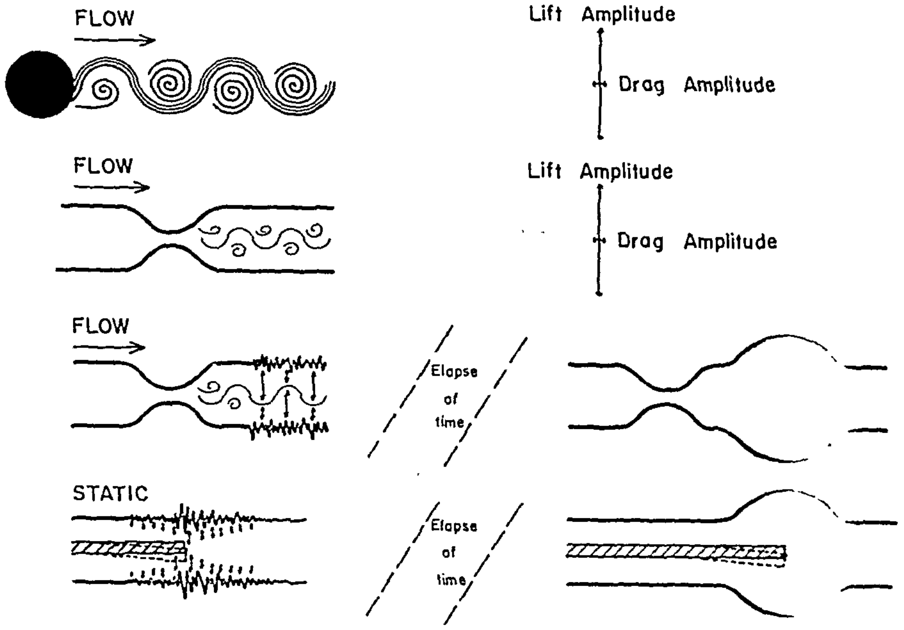

Fig. 2.—Diagram of the theoretical basis of the production of murmurs, thrills and post-*stenotic dilatation.* With flow past a wire or cylinder, vortices are shed which cause periodic pressure fluctuations in the wake. The bulk of the energy is radiated in a direction perpendicular to the flow (the lift amplitude) rather than parallel to the flow (the drag amplitude). Flow through a stenosis is a modification of this basic pattern. The energy of the pressure fluctuations is of the order of acoustical intensities and, if strong enough, will be transmitted to the vessel wall, causing it to vibrate. With time this could lead to structural fatigue of the elastic tissue, with dilatation the result. Experimentally, a vibrating blade can reproduce these physical forces. By using a static tube, physical forces due to fluid flow can be eliminated and the effectiveness of vibrational fatigue more clearly tested. In practice, the point of maximal vibration of the tubing wall was usually found to be 0.5 cm. proximal to the blade tip.

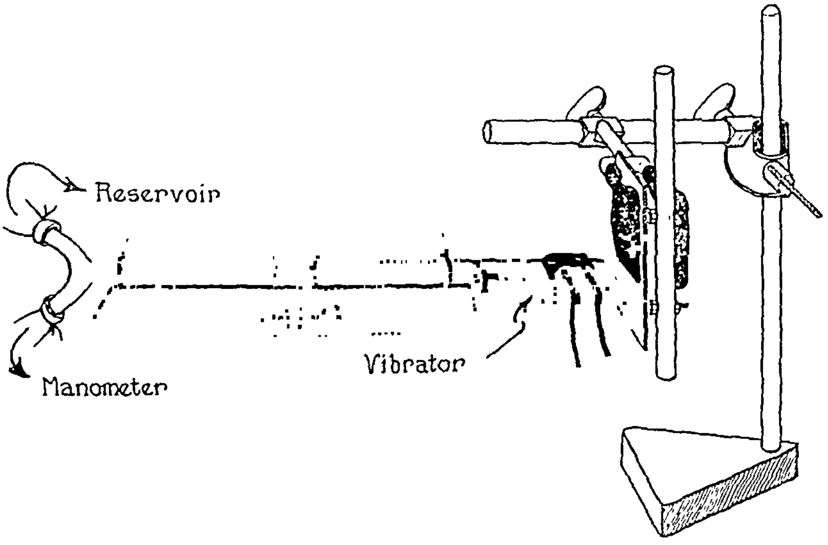

Fig. 3.—Diagram of apparatus used.

by stroboscopic illumination and was found to be 96 cycles per second The blade was so placed that it did not touch the tubing wall. Thus, the energy of the vibration was transmitted through water to the elastic walls. The region of maximum vibration was found to be approximately 0.5 cm. proximal to the blade tip. Thus, all but two factors that may cause wall damage were eliminated. Only a hydrostatic pressure load and periodic pressure fluctuations, roughly of the magnitude of acoustical intensities, were the forces applied This arrangement, we felt, approximated the physical factors to be tested which are found in the region in which post-stenotic dilatation occurs.

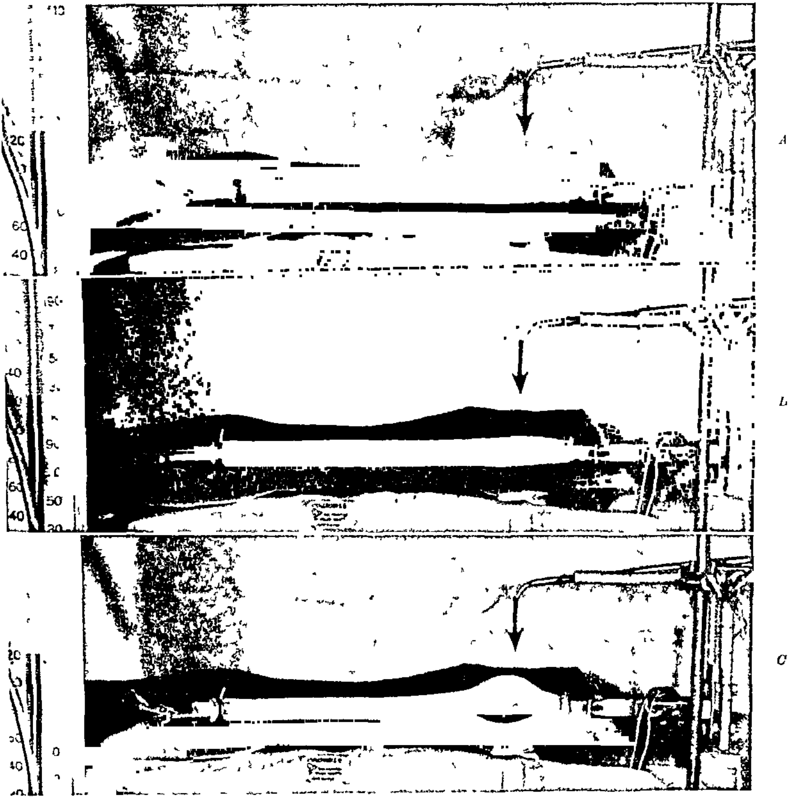

Fig 4.—The tube after (A) 1 hour of vibration, (B) 8 hours of vibration, and (C) 10 hours of vibration the tubing wall is weakened to the degree that it can no longer support the original hydrostatic pressure load of 130 mm Hg.

Ten tubes, of varying quality, were placed under constant hydrostatic pressure which varied from 130 to 140 mm. Hg. After from 7 to 120 hours, a moderate dilatation was noted in the tubing wall in the region subjected to vibration. Within 5 hours after this occurred, the stressed segment was unable to withstand the original hydrostatic pressure and progressive dilatation was noted (Fig. 4). It was discovered that the higher static pressures led to earlier dilatation.

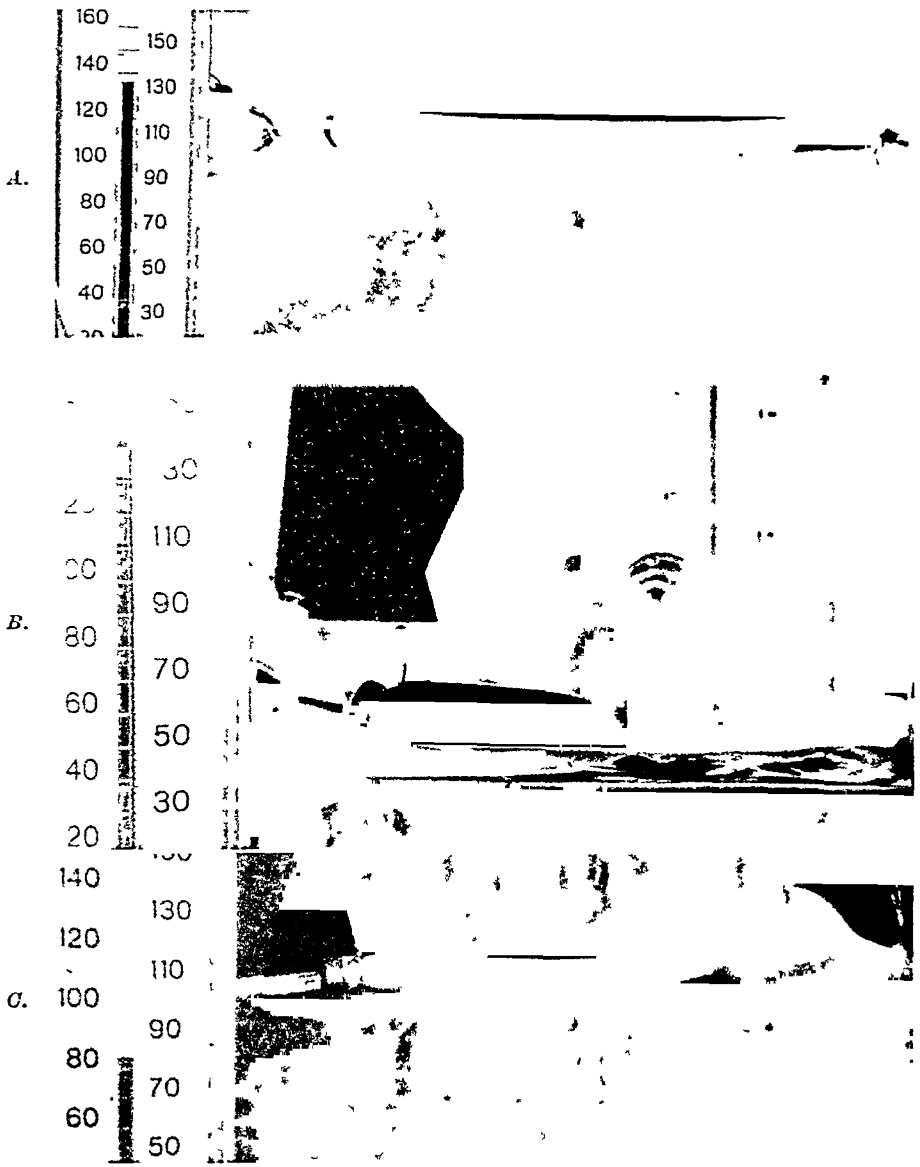

Fig. 5.—*A*, Tube under static pressure of 135 mm. Hg after 185 hours. *B*, Tube during compression after 65 hours *C*, Tube after 30 hours of vibration; the original pressure load was 130 mm. Hg A line marks the point of maximum vibration

Five tubes, not subjected to vibration, were placed under very high hydrostatic pressures. These ranged from 190 to 240 mm. Hg. At these pressures, the strength of the material would be exceeded and dilatation would occur at one or the other end of the tube. It was noted that this dilatation occurred at a distance of from 2.25 to 3.5 cm. from the point of fixation. The fact that the tube dilated at this constant location suggested that fixation of the tube had some part to play in the site of weakening. However, the vibrating blade was so placed in the ten tubes previously mentioned, that the point of maximum vibration was 4 cm. or more from the point of fixation.

To exclude further the possibility that the tube with time would have dilated at this point without vibration the following modifications were made. The vibrating blade was lengthened until the point of maximal vibration could be felt at a point 9.5 cm. from where the tube was fixed about the stopper. After 10 hours, dilatation occurred at this point. We were unable to extend the length of the blade beyond this point as nodes developed which gave several points of nearly equal vibration and thus did not permit a concise experiment.

In order to test the relative effect of the various factors that may be involved in post-stenotic dilatation, the following experiment was performed Short segments of tubing from adjacent areas were cut. One segment was subjected to a static pressure of 135 mm. for 185 hours without the appearance of dilatation. Another tube was compressed by a plunger, and the pressures in this tube varied from 138 to 142 mm. Hg at maximum compression. This is not a wide range of pressures; however, the short segment of tubing was found to dilate 2.3 mm. Hg during each compression stroke, representing considerable stretch. After 65 hours no dilatation was noted. A third segment was subjected to 130 mm. Hg and, after 30 hours of vibration, dilatation was observed at the point of maximum vibration (Fig. 5).

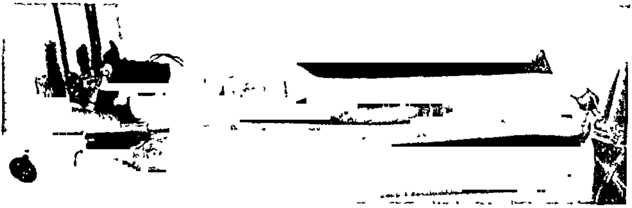

Fig. 6.—Matched tubes after 104 hours. Upper tube was subjected to vibration. A line marks the point of maximum vibration The lower tube, not subjected to vibration, did not show local dilatation after 2 weeks.

Because of the wide range of time required to produce dilatation, tubing produced by one manufacturer (Duval) was used in the last experiment. Matched sections were cut from the middle of the standard 90 cm. lengths. Each pair of tubes was placed under the same hydrostatic pressure load. One of the pair was subjected to vibration, the other was not. Four tubes at from 135 to 140 mm. Hg dilated at the point of maximum vibration in from 73 to 115 hours. The respective pairs showed no dilatation after 2 weeks (Fig. 6). Another tube at 130 mm. Hg dilated after 580 hours of vibration. A matched section at the same pressure did not dilate after 2 months. This experiment demonstrated that the vibratory stress appears to be the one of greatest significance.

DISCUSSION

Many theories have been proposed which have sought to explain the development of post-stenotic dilatation on the basis of physical principles. Campbell and Kauntze[5] have postulated that post-stenotic dilatation in aortic stenosis can be largely explained by the relative elevation of lateral pressure in the region downstream from the stenosis (the Bernoulli principle). They recognized, however, that the very low downstream pressure in pulmonary stenosis made this explanation less plausible. They also felt that the presence of post-stenotic turbulence may be another factor in the development of post-stenotic dilatation.

Holman[1] was the first to submit the question of post-stenotic dilatation to exhaustive physical analysis. He emphasized the importance of considering the factors of physical stress which lead, in time, to structural fatigue of the vessel wall. He felt that the high velocity jet of blood issuing from the stenosis was suddenly retarded by the slow moving stream distal to the stenosis, causing a local conversion of kinetic energy into lateral pressure. In addition, this process led to the development of eddies of turbulent flow and reversed flow which struck the vessel wall and led to its vibration. He felt that the sites of the production of a local high lateral pressure and greatest turbulence were the same, and that at this place the point of maximum dilatation was found.

Robicsek[6] and his colleagues studied the problem and could find no experimental or clinical evidence of a "local increase" of the lateral pressure in the post-stenotic region. By injecting dye into a glass model of a stenosis with a post-stenotic dilatation, they demonstrated that there was maximum turbulence in the distal end of the dilated region (Holman, by the same technique, had also demonstrated the presence of turbulence in the area of post-stenotic dilatation). They felt, then, that turbulence was an acceptable explanation of the weakening of the vessel wall and the consequent development of post-stenotic dilatation. However, they accepted the "possibility that the cavitation process is perhaps the most important factor in producing the anatomic phenomenon known as poststenotic dilatation by injuring the wall of the blood vessel."

It is difficult for us to understand why a model of already existing post-stenotic dilatation was chosen to demonstrate the presence of turbulence. This may have been the cause of Robicsek's dye injection study showing that the region of maximal turbulence is not at the site of maximal dilatation but, rather, at the point where dilatation has decreased to almost the normal vessel caliber. Be that as it may, the theory that turbulence could lead to post-stenotic dilatation appears even less likely when one realized that it is very probably incapable of producing pressures even of the order of acoustical strength. To ask that turbulence set the vessel wall into vibration seems to be an unreasonable demand.

When, however, one considers that the wake in blood can be made to fluctuate pressure-wise in a nearly periodic fashion due to the presence of an obstacle or narrowing in the vessel wall, then it appears reasonable that a force is present capable of producing a murmur. If large enough, this force will be manifest as a thrill It appeared to us that this was the factor to investigate, as of all the possible sources of unusual stress on the downstream wall of the vessel, the murmur (and thrill) is the only one present, and present in maximal intensity, in the region in which one notes post stenotic dilatation In this connection, Spencer[7] and his colleagues have shown that murmurs of coarctation, recorded directly from the aorta, are maximal in intensity in the region of greatest post stenotic dilatation

In regard to the question of cavitation, it should be briefly noted that work in this laboratory has shown that it will not occur in blood unless the driving pressure is at least 350 mm Hg As pressures of this magnitude are rarely, if ever, encountered in the body it seems that this is an unlikely explanation of post stenotic dilatation

These experiments were performed with thin walled rubber tubes and with energies which approximated those which might be found with a loud murmur and a moderately intense thrill It may be that the relatively thick walled vascular structures would be able to withstand these stresses and not tend to dilate This report, however, suggests that vibration of discrete segments of distended elastic tubes can lead to dilatation in that area The fixation of the tubes to a solid surface undoubtedly contributes to the dilatation, but appears to be less significant than vibration

It is hoped that this work has offered a satisfactory physical basis for post stenotic dilatation consistent with the known physiologic and clinical characteristics of the phenomenon

SUMMARY

The physical factors which may play a part in the development of post-stenotic dilatation are re examined Factors relating to pulsatile flow are found to be unlikely causes A new theory of murmurs is applied and the hypothesis is made that vibrations of the vessel wall (thrills) are of sufficient energy to cause structural fatigue and dilatation This was demonstrated by subjecting latex rubber tubes held under a static pressure to vibration

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(For Discussion, see page 703)

THE PATHOLOGIC EFFECTS OF METALLIC FOREIGN BODIES IN THE PULMONARY CIRCULATION

A Long-Term Experimental Study

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INTRODUCTION

The surgical management of the asymptomatic metallic foreign body lodged in the pulmonary arterial circulation poses a difficult problem because of the paucity of reports and diversity of opinion. However, it is probable that this condition is not as rare as is recorded for we know of several unreported cases. When hemorrhage or infection is present there is a clear-cut indication for the removal of the foreign body. Yet when the foreign body is asymptomatic and has produced no significant pulmonary changes on the chest roentgenogram, the advisability of a thoracotomy to remove this foreign body is open to question. We have been faced with this problem clinically and it is possible in one instance that we removed a foreign body from a branch pulmonary artery unnecessarily. Since World War II, potential infection, hemorrhage, emboli, and septicemia have been cited as indications for removal of the asymptomatic foreign body. Considerable support for this point of view may be found in the medical literature.[1, 5, 8, 9, 10] The justification for the prophylactic removal of asymptomatic foreign bodies has been based on what seems to be logical theoretical considerations. However, except for sporadic cases, neither long-term clinical nor experimental studies concerning the fate of foreign bodies in the pulmonary arteries are available.[2, 6] Thus, this series of experiments was undertaken to determine ultimate effects of metallic foreign bodies introduced into the pulmonary arterial circulation and the systemic circulation of mongrel dogs under varying conditions up to a period of 2 years.

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METHOD

A total of 66 foreign bodies was introduced into the superior vena cava or directly placed in the main pulmonary artery in 42 mongrel dogs (Table I). To compare the reaction of the pulmonary artery to that of systemic vessels, a series of 14 metallic foreign bodies were introduced into the common iliac arteries of dogs. Large mongrel dogs weighing from 15 to 35 kilograms were employed. Lead fragments from 15 to 20 mm. in longest dimension, 22- and 38-caliber lead bullets, and fragments of needles were used.

TABLE I. INTRAVASCULAR FOREIGN BODIES

SITE	NO. OF FOREIGN BODIES	NO. OF DOGS	MORTALITY
Right atrium	4	4	0
Right ventricle	1	1	0
Main pulmonary artery	8	7	4
Branch pulmonary artery	53	28	1
Common iliac artery	14	14	0
Totals	80	42	5

Employing positive pressure ether anesthesia, the chest was opened under aseptic conditions. Lead bullets and fragments were then introduced into either the superior vena cava or the main pulmonary artery. In some of the animals the foreign bodies were introduced into the common iliac arteries immediately following the completion of the thoracotomy. Roentgenograms and gross and microscopic studies of the effects of the foreign bodies were made at periods of time varying from the day of operation up to 48 months.

RESULTS

Fate of Foreign Bodies Introduced Into the Superior Vena Cava.—

At the beginning of our experiments, foreign bodies to produce pulmonary embolization were introduced directly through the azygos vein into the superior vena cava and forced into the right atrium. This method was chosen since it is the usual manner in which foreign bodies enter the pulmonary circuit. After a study of 15 such experiments, we found, in a third of the cases, the foreign body lodged in the right atrium or right ventricle and two thirds of them lodged in the pulmonary arterial circulation. The foreign bodies in the right side of the heart were well tolerated.[6] By the third week they were completely covered with endothelium and caused no erosion or embolization in observations extending over 20 months.

Pulmonary and Systemic Arterial Reaction to Foreign Bodies.—

In none of the 61 instances in which a foreign body was introduced into the pulmonary artery and in the 14 times that a foreign body was introduced into the common iliac artery did erosion of the vessel, secondary hemorrhage, or infection take place (Table II). In the pulmonary artery, minimal clotting

TABLE II. REACTION OF PULMONARY AND ILIAC ARTERIES TO METALLIC FOREIGN BODIES

	NO.	EROSION	PROXIMAL CLOT	DISTAL CLOT
Main pulmonary artery	8	0	0	0
Branch pulmonary artery	53	0	0	0
Common iliac artery	14	0	6*	6*
Totals	75	0	6*	6*

*Slight.

occurred the first 2 or 3 days after the injection of a foreign body but no massive clotting occurred either proximal or distal to the foreign body. There was a rapid encasement of the foreign body by organization of the clot and growth of the intima of the vessel to cover the ends of the foreign body which was encased in this fibrous cocoon or capsule. This reaction, which we have not found reported before, appears to be similar to that shown by the growth of endothelium in the lining of vessel substitutes. In the common iliac artery in dogs, there is an excellent collateral blood supply due to the fact the dog has an additional large caudal artery extending from the mid-portion of the bifurcation of the aorta downward. Foreign bodies in the common iliac arteries of dogs showed a response to the foreign body similar to that observed in the pulmonary artery. This reaction is due to the fact that there is an excellent collateral circulation preventing massive clotting distal to the

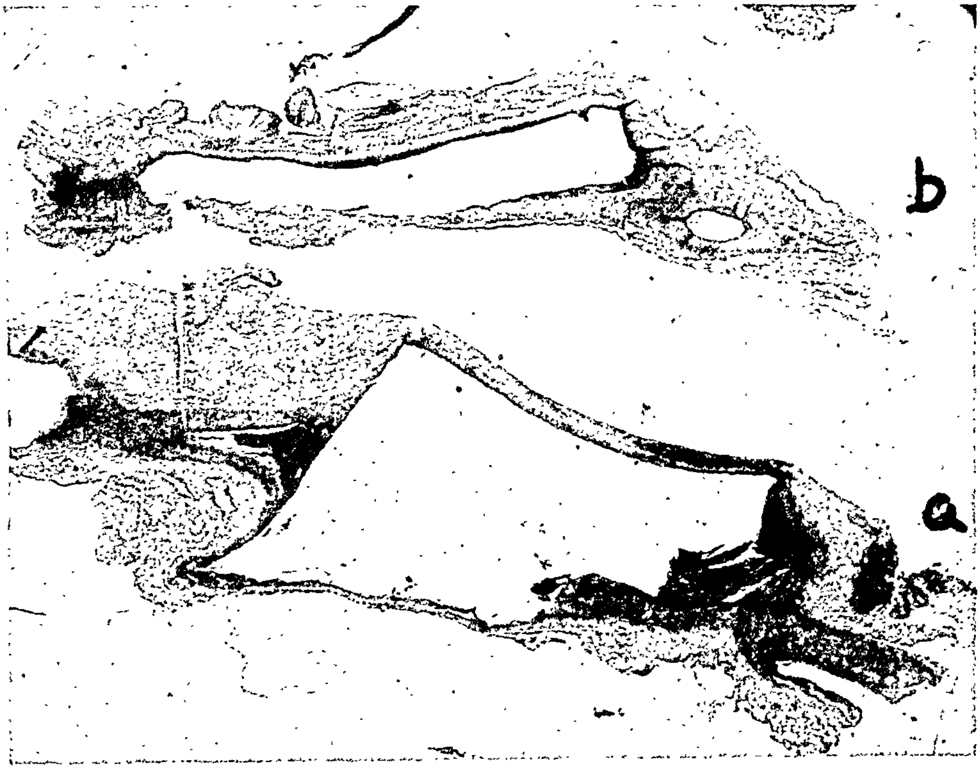

Fig. 1.—Dog 478. Longitudinal low-power section of left main pulmonary artery and right common iliac arteries 3 days after embolization of lead foreign bodies. *a*, Left main pulmonary artery. *b*, Left common iliac artery. Both vessels show early organization of small clot proximal and distal to the foreign body.

foreign body. The bullet is well encased in 10 days' time, and shows very little change in periods of observation up to 2 years.

Fig. 1, *a* shows a pulmonary artery 8 days after the implantation of a 38-caliber lead bullet. The reaction is similar to that presented in Fig. 1, *b*, which shows the common iliac artery where a 22-caliber bullet was lodged. Three days after implantation, one notes early organization of the clot. By the end of the second week the fibrous capsule is complete and thereafter shows very little change. Fig. 2, *a* shows a low-power photograph of the pulmonary artery, 18 months after implantation of a foreign body. Comparable findings are seen in Fig. 2, *b*, which shows the reaction to a foreign body in the common iliac artery implanted 18 months previously. In both instances the foreign body has been completely isolated in a fibrous and endothelized cocoon. The blood supply to the leg was excellent and organized clot was seen for a distance of 1 cm. to 1.5 cm. on the proximal and distal sides of the "encysted" foreign body.

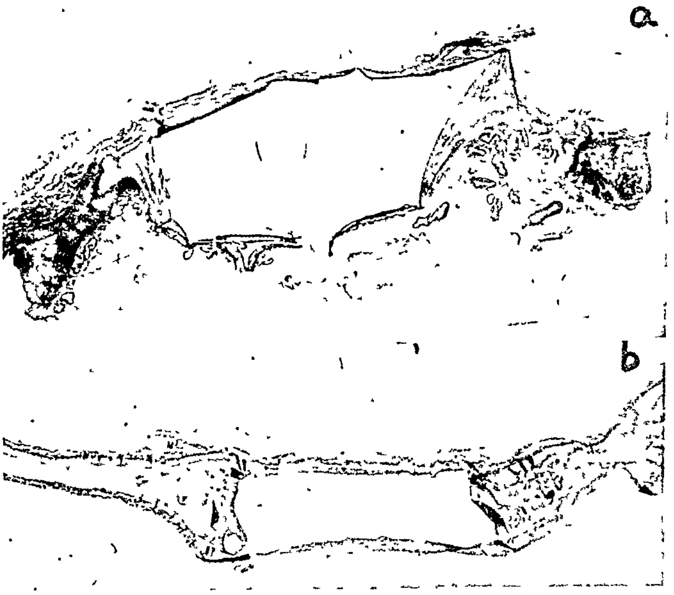

Fig 2—Dog 487 Longitudinal section of left lower lobe pulmonary artery (*a*) and left common iliac artery (*b*) 18 months after embolization of lead foreign body Both vessels show foreign body in vessel completely surrounded by a "cocoon" of dense connective tissue Adjacent to this the obstructed portions of the vessel have become endothelized

Reaction of Lung to Foreign Body in a Branch Pulmonary Artery.—

A total of 53 metallic foreign bodies, 41 lead bullets and 12 needle fragments were introduced into branch pulmonary arteries under the above conditions, in a series of 28 dogs. With the large lead foreign bodies there was blanching of the involved lobe immediately after implantation. However, in half an hour the affected lobe became as pink as the uninvolved lobe. In 48 instances the lobe appeared to be grossly normal, whereas in five experiments gross infarcts were noted (Table III). For the most part, the lung appeared normal to external examination and inflated well. However, on microscopic examination a fairly severe pathologic change was present soon after embolization of the foreign body: extravasation of red blood cells, edema, and thickening of the alveolar walls in the pulmonary tissue distal to the foreign body. Fig. 3 shows this reaction in the left lower lobe of the lung 2 days after the introduction of foreign body in the pulmonary artery of the left lower lobe. The intra-alveolar fluid and red blood cells were absorbed slowly and considerable variation was seen in the rate of absorption. There is no further improvement in the appearance of the lung noted in the period from 6 months to 2 years. Fig. 4 shows the microscopic appearance of the lung 18 months after the implantation of a foreign body in the pulmonary artery of the left lower lobe. Considerable areation of the lung has taken place as compared with the findings in Fig. 3, although perivascular and peribronchial thickening are noted.

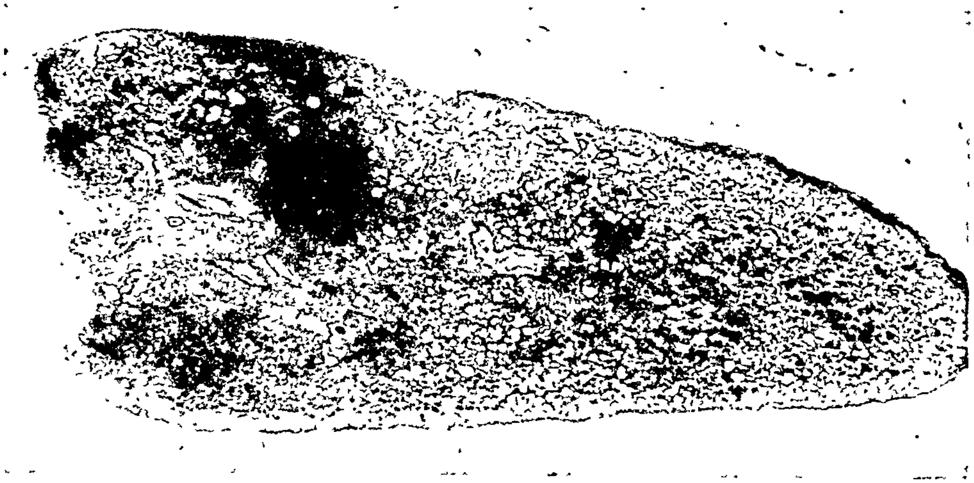

Fig. 3.—Dog 474. Peripheral section of left lower lobe of lung 2 days after embolization of lead foreign body to left lower lobe pulmonary artery. The alveoli are filled for the most part with fluid and red blood cells.

TABLE III. PULMONARY REACTION TO FOREIGN BODY IN BRANCH PULMONARY ARTERY (53)

NO. OF DOGS	TIME	BILATERAL OPERATION	MULTIPLE F.B.	GROSS INFARCT	GROSS EDEMA	GROSS FIBROSIS	RESULT
7	1- 7 da.	3	3	2	1	0	1 died*
3	8-28 da.	1			1		Sacrificed
8	1- 3 mo.	1	3	1	1		Sacrificed
5	4- 6 mo.			1	2		Sacrificed
3	6-12 mo.	2	2				Sacrificed
3	12-24 mo.			1			Sacrificed
29		7	8	5	5	0	1

*Aspiration pneumonia.

Surprisingly little effect was seen in the roentgenogram with the foreign body in a lobar or segmental artery. However, slight infiltration was noted without gross lobar density or infiltration. Fig. 5 demonstrates a foreign body in a lobar pulmonary artery 1 month after implantation without gross evidence of pulmonary reaction in the chest roentgenogram. In Fig. 6, the lateral roentgenogram taken 18 months after the implantation of a foreign body in the left lower lobe artery shows minimal peribronchial thickening.

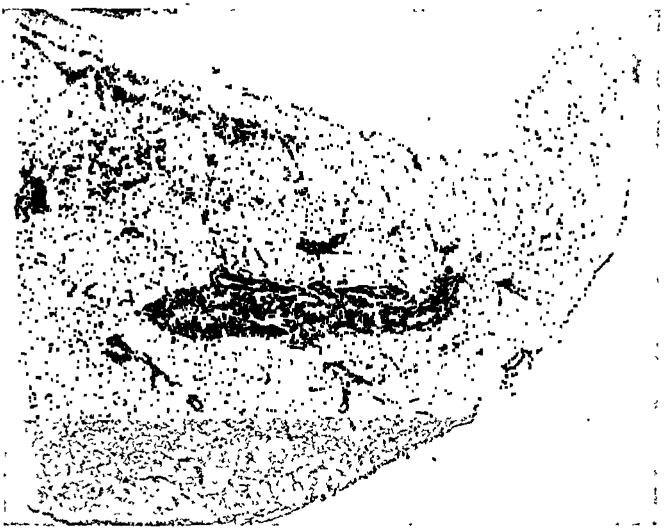

Fig. 4.—Dog 487. Peripheral section of left lower lobe of lung 18 months after embolization of lead foreign body to left lower lobe pulmonary artery. Pulmonary tissue well aerated. Perivascular and peribronchial thickening is present.

Reaction of Lung to Foreign Body in Main Pulmonary Artery.—

Experience with a foreign body occluding the main pulmonary artery was accumulated with some difficulty because even large foreign bodies tend to migrate to the branch pulmonary artery. We believe that it is true clinically that most foreign bodies entering the pulmonary circuit will migrate to a branch artery. It is logical that foreign bodies that do not occlude the lumen of the main pulmonary artery will be propelled distally by the current of blood and arterial pulsation to a point where the artery is blocked. In all of the foreign bodies involving the pulmonary artery in the experiments of Fritz and his colleagues,[6] the foreign body was lodged in a branch pulmonary artery. However, in the authors' experiments there were 8 dogs in which a large foreign body was retained in the main pulmonary artery (Table IV).

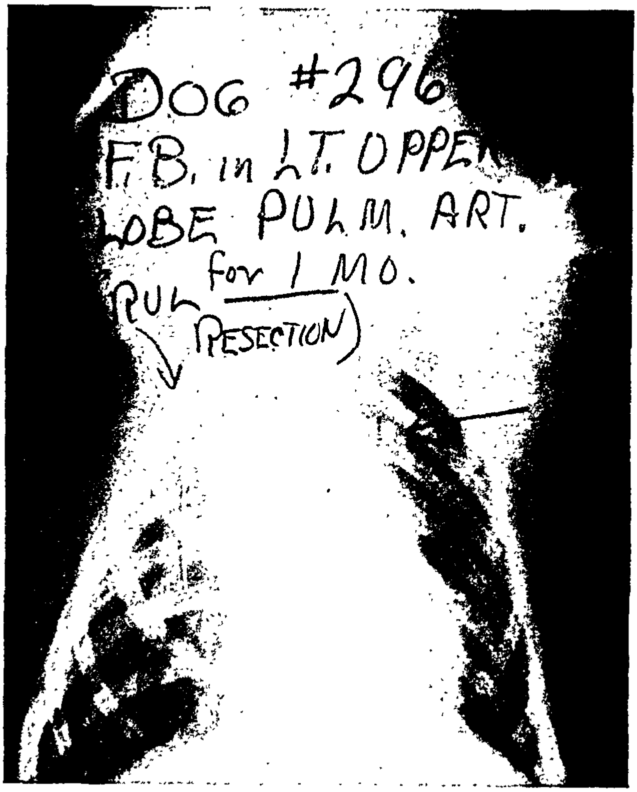

Fig. 5.—Dog 296. Roentgenogram of chest made 1 month after lead foreign body had been embolized to left upper lobe. Right upper lobe had also been resected. Lung field distal to foreign body appears normal.

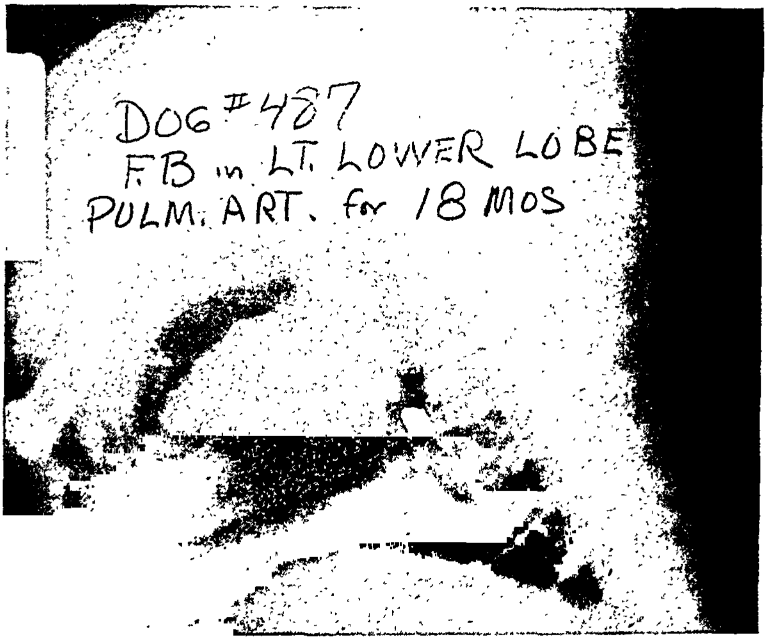

Fig. 6.—Dog 487. Roentgenogram of chest made 18 months after lead foreign body embolized to left lower lobe pulmonary artery. Lateral view shows slight peribronchial thickening.

TABLE IV. PULMONARY REACTION TO FOREIGN BODY IN MAIN PULMONARY ARTERY

DOG	DAYS	GROSS INFARCT	GROSS EDEMA	GROSS THROMBOSIS	RESULT
300	1	yes	yes	no	Died; anesthetic reaction
453	1	yes	yes	no	Died; auricular fibrillation
312	1	yes	yes	no	Died; cardiac manipulation
472	4	yes	yes	no	Sacrificed
468	10	yes	yes	no	Sacrificed
455	24	yes	yes	no	Died; bilateral foreign bodies; hypoxia
482	55	yes	yes	no	Sacrificed
342	13 mo.	yes	yes	no	Sacrificed

The entire lumen of the artery was blocked and marked changes in the lung were noted. The reaction of the lung was immediate and severe in all of the 8 animals. The lung was engorged, edematous, appearing grossly to be infarcted. Later fibrosis and organization of the lung and some areation had taken place. These observations paralleled the previously reported experiments in which the main pulmonary artery had been ligated.[11, 13] Even though the bronchial artery will keep the lung alive, the anatomic changes come on rapidly and are much more marked with the main pulmonary artery obstructed, than when a branch pulmonary artery is blocked. Fig. 7 demonstrates the severity of the pulmonary reaction on a low-power section of distal pulmonary tissue 4 days after the implantation of a foreign body in the main pulmonary artery. This reaction was slow to subside after the impingement of the foreign body. The roentgen findings were dramatic and showed evidence of the marked pathologic changes that were taking place in the lung, deprived of its pulmonary artery blood supply. In 1 month's time, the chest roentgenogram shows a dense shadow occupying the major part of the affected lung (Fig. 8). In 20 months, very little increased areation has taken place on the chest roentgenogram, shown in Fig. 9. This reflects the pathologic changes in the lung in which considerable fibrosis has taken place with

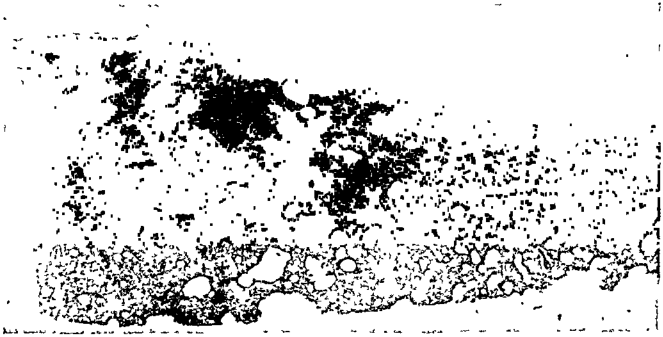

Fig. 7.—Dog 472. Peripheral section of left lower lobe of lung 4 days after embolization of lead foreign body fragment to left main pulmonary artery which was completely blocked. The lung is practically airless. The alveoli are completely filled with fluid and red blood cells.

thickening of the interalveolar partitions which in some places present an almost solid airless lung. Thus, although the lung remains viable it is obviously damaged and appears to have little if any function. One of the females delivered multiple litters of puppies and 1 dog escaped from his cage and fought and killed another dog the day after the implantation of the foreign body. Yet in spite of the marked reaction to the foreign bodies in the main pulmonary artery, practically all of the dogs tolerated them very well.

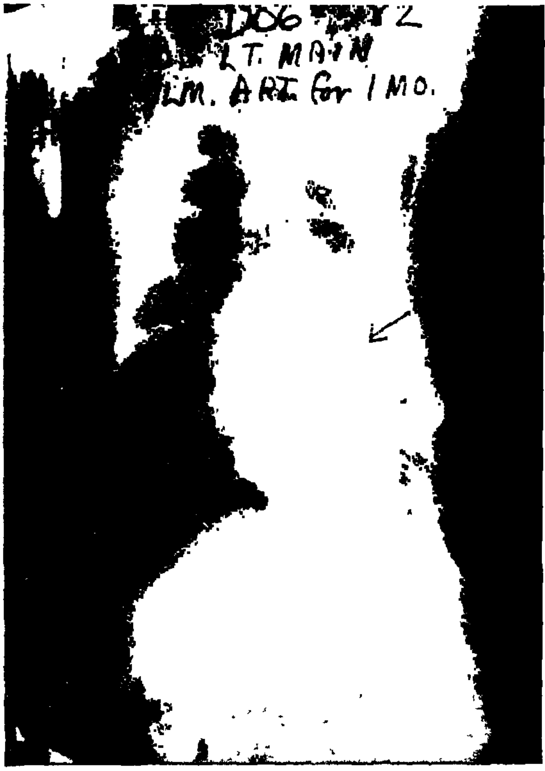

Fig. 8.

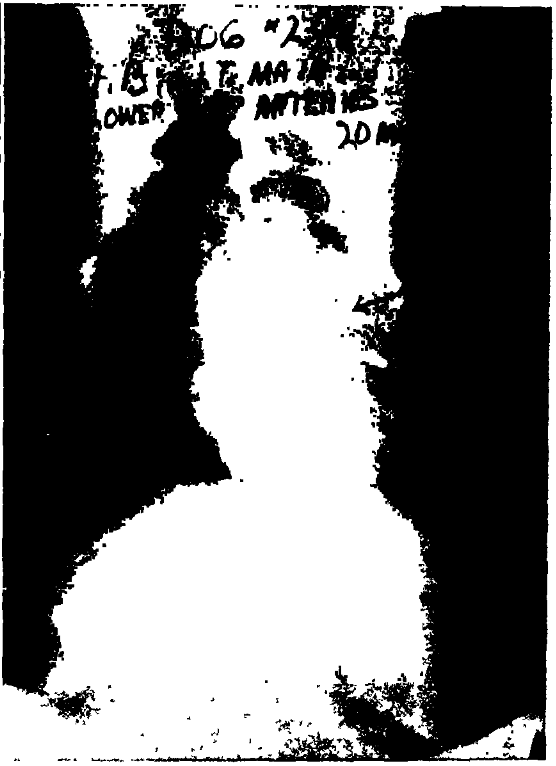

Fig. 9.

Fig. 8.—Dog 482. Roentgenogram of chest made 1 month after lead foreign body embolized to left main pulmonary artery. Left lung almost completely opaque, reflecting severe pulmonary infarction.

Fig. 9.—Dog 298. Roentgenogram made 20 months after embolization of lead foreign bodies to left main and lower lobe pulmonary arteries. Some aeration of base of lung and slight aeration at apex. Remainder of lung opaque.

Role of the Bronchial Artery.—

It has been long known that the bronchial arteries play an important part in the blood supply of the lung. In some congenital cardiac anomalies accompanied by severe pulmonary stenosis or absence of the pulmonary artery, the entire blood supply may come from the bronchial arteries. Considerable experimental work has been done on the importance of the bronchial blood supply to the lung.[3, 12, 13] In all the dogs in which foreign bodies were introduced into the pulmonary arterial circulation, the bronchial arteries were engorged and dilated (markedly so in some instances).

The role of the bronchial arteries was studied in a series of 5 dogs in which the bronchial arteries of the main bronchi were divided at the time a foreign body was introduced into a branch pulmonary artery. Reaction of the lobes to this double impairment of the blood supply was seen in severe pulmonary infarction, edema, and extravasation of blood cells. This came on early and was slow to resolve. In the animals with foreign bodies in the lobar pulmonary artery, the reaction of the lung was similar to that seen when foreign bodies lodged in the main pulmonary artery. This difference is shown in Fig. 10, *a* and *b*. Fig. 10, *a* (Dog 370) shows the effect of the foreign body placed 11 months previously in the left lower lobe branch of the pulmonary artery. The lung is well areated and the architecture is preserved. Fig. 10, *b* shows the reaction to the foreign body placed in the opposite lower lobe pulmonary artery of this same animal in which the bronchial arteries had been ligated at the time of the introduction of the foreign body. It is noted in Fig. 10, *b* that the microscopic pathologic changes are much more severe than in the lower lobe of the opposite side. In these cases the lung did not become completely gangrenous, indicating that either the intramural branches of the bronchial arteries provided some blood supply or that communicating channels existing between the lobes were sufficient to maintain the life of the lung tissue distal to the foreign body and the ligation of the bronchial artery. Intrapleural adhesions of a vascular type were not noted, so blood supply from this source seems unlikely.

The injection of a suspension of fine particulate carbon (lampblack) into the aorta just prior to the sacrifice of the animals was of considerable interest. Carbon could be readily identified in the lung distal to the foreign body, whether the main pulmonary artery or the branch pulmonary artery had a foreign body. The carbon was seen in branch bronchial arteries and appeared to reach the pulmonary tissue via bronchial pulmonary arterial communications. Fig. 11 shows diffuse pulmonary capillary embolization with the carbon particles in the lower lobe of the lung in which a foreign body had been placed in the main pulmonary artery 13 months previously. The severe pulmonary reaction of the lung distal to the foreign body in the main pulmonary artery consists of alveolar septal thickening, peribronchial and perivascular fibrosis in the partially aerated lung. These are the typical final pathologic changes seen in the lung 6 to 24 months after a foreign body occludes a main pulmonary artery. However, since the pulmonary capillaries are diffusely embolized with particulate carbon, it appears that bronchial pulmonary arterial communications are fairly extensive. They are a potent source of blood to the lung tissue distal to a foreign body in the pulmonary artery. Bloomer and associates have shown that it is possible for the lung to maintain some respiratory function through the bronchial blood supply after pulmonary artery ligation.

Effect of Systemic Pulmonary Artery Anastomosis.—The pulmonary artery pressure is low, being from [illegible] that of the systemic circulation. The question arose if a systemic artery were anastomosed to the main pulmonary artery proximal to the foreign body, would the lung be better nourished with this increased circulation from the

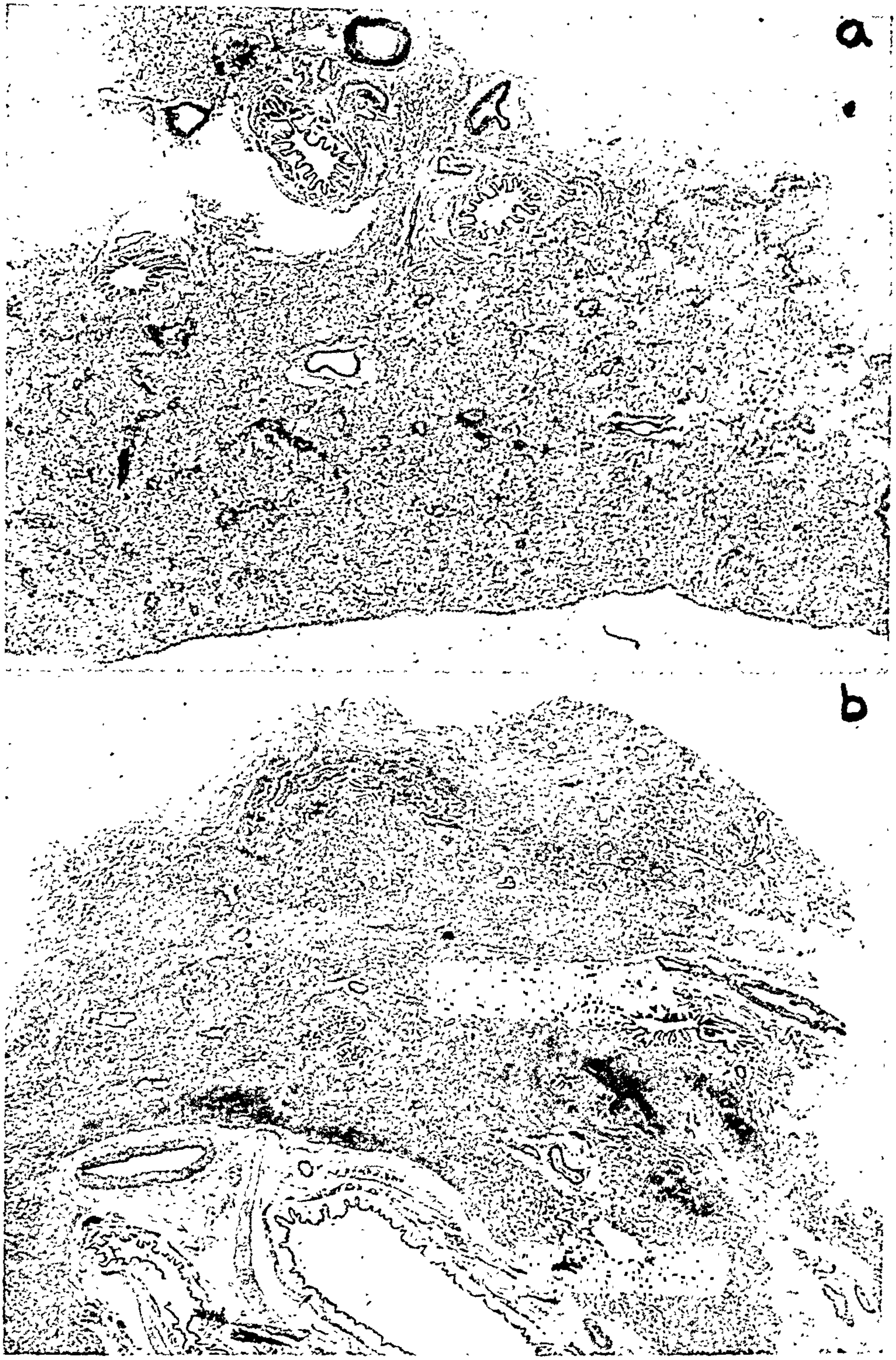

Fig. 10.—Dog 370. *a*, Peripheral section of left lower lobe of lung 11 months after impingement of lead foreign body in left lower lobe artery. Lung is well aerated and architecture preserved.

b, Peripheral section of right lower lobe of lung 11 months after impingement of lead foreign body and division of bronchial arteries. Marked interalveolar, perivascular, and peribronchial infiltration and fibrosis is noted. Lung tissue is practically airless. Reaction similar to that caused by main pulmonary artery embolization.

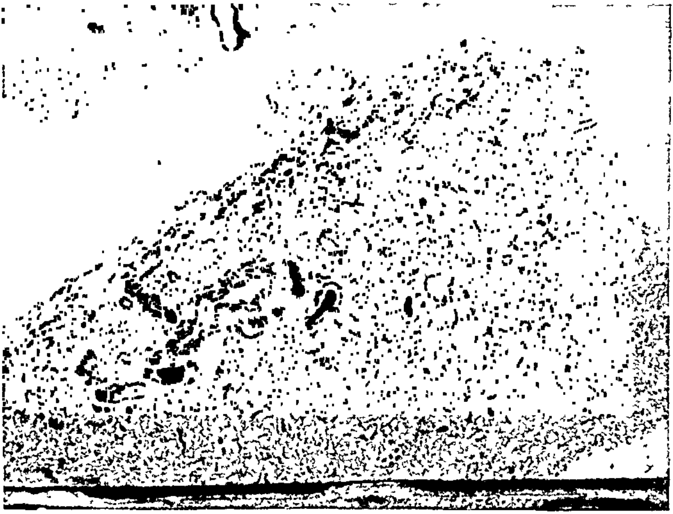

Fig 11 —Dog 312. Peripheral section of right lower lobe of lung 13 months after embolization of lead foreign body in right main pulmonary artery. Fine carbon pigment injected into aorta is seen in bronchial arteries and diffusely filling pulmonary capillaries. Considerable aeration of lung has taken place but interalveolar thickening and perivascular and peribronchial thickening are present.

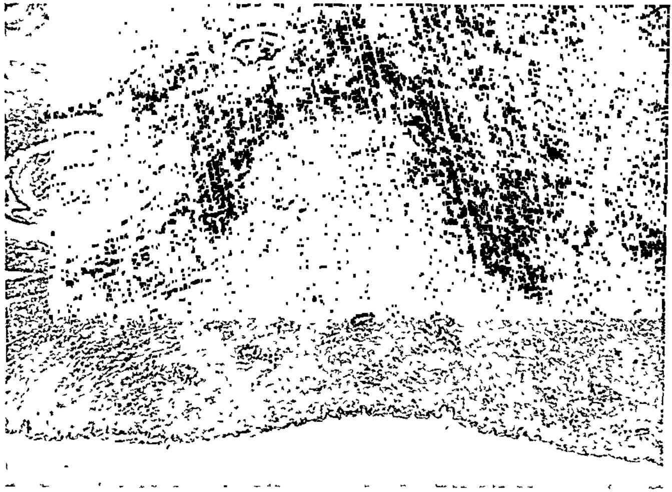

Fig. 12 —Dog 369. Section of left lower lobe of lung distal to lead foreign body embolized to left lower lobe 4 months previously. Anastomosis of subclavian artery to pulmonary artery has resulted in a flooding of the lung with blood Fibrosis and lack of aeration is noted 4 months later.

systemic arterial anastomosis? In four instances, the left subclavian artery was anastomosed to the pulmonary artery. Marked engorgement of the entire lung occurred with severe congestive changes and hemorrhage into the alveoli. The effect of the increased pressure and blood flow in the pulmonary circulation was striking, and the engorgement and hemorrhage into the lung were the same above as below the level of the foreign body in the pulmonary artery, indicating a marked flooding of the lung through pulmonary arterial capillary anastomoses (Fig. 12). In fact, similar and almost severe changes were noted in the opposite lung. Thus, it is apparent that the severe engorgement and hemorrhage in the lungs caused by the high pressure and blood flow from a systemic artery precluded the use of such an anastomosis as a means to increase the pulmonary alveolar flow to the lung distal to the foreign body.

SUMMARY

In 42 dogs in which 80 foreign bodies were introduced into the superior vena cava, pulmonary artery, or common iliac arteries, there was only one death due to the introduction of the foreign body in a long-time study covering periods up to 2 years. This death occurred in a dog who had a foreign body in the left main pulmonary artery and the right main pulmonary artery, together with a right upper lobe lobectomy. Asphyxia was apparently the cause of the death.[7]

These metallic foreign bodies were well tolerated and no erosion, hemorrhage, or secondary infection occurred and the foreign body was rapidly covered with an endothelized cocoon. Proximal or distal clotting in the pulmonary artery was not noted. A similar reaction was seen in all 14 experiments following the introduction of metallic foreign bodies in the common iliac arteries of dogs in which an excellent collateral blood supply was present.

The lung distal to a foreign body in the lobar or segmental pulmonary artery was grossly aerated and showed some gross infarction in only 5 of the 51 foreign bodies introduced into a lobar artery. The lung appeared grossly normal in all but five instances and roentgenograms were clear or showed minor changes. However, on microscopic examination of the lung, congestion, hemorrhage, and thickening of the alveoli with edema were noted soon after the embolization of the foreign body. In a period of from 6 months to 2 years, these changes gradually cleared microscopically although slight peribronchial and perivascular fibrosis persisted.

On the other hand, foreign bodies in the main pulmonary artery produced severe congestion, hemorrhage, and edema of the entire lung which appeared to be grossly infarcted. X-ray studies showed diffuse consolidation of the lung persisting for months after the blocking of the main pulmonary artery. In 2 years' time, the lungs never completely cleared although there was some aeration of the lung ,and the lung decreased in size. Considerable fibrosis was present. There could be little if any pulmonary function of the distal lung with the pulmonary artery (either main or branch) blocked by a foreign body Davis and co-workers[4] have shown that the main pulmonary artery may be occluded for periods up to 48 hours and the pulmonary changes will be reversed by re establishment of the pulmonary circulation After this period of time, irreversibility of change was the rule

Bronchial arteries have an important role in supplying blood to the lung distal to a foreign body in the pulmonary circulation Much more reaction of the lobe with bronchial artery divided was noted as compared with the bronchial artery intact Fine carbon suspensions injected into the aorta may be seen diffusely filling the bronchial and pulmonary capillaries distal to a foreign body in the pulmonary arterial circuit Anastomosis of a systemic vessel (the subclavian artery) to the pulmonary artery embolized by a foreign body does not prevent pathologic changes in the lung distal to the foreign body In fact, the pulmonary engorgement, hemorrhage, and edema were so severe as to contraindicate this procedure

CONCLUSIONS

1 In the introduction of 61 foreign bodies to the pulmonary circulation in no case was there hemorrhage, erosion of the vessel wall, secondary infection caused by the foreign body The foreign bodies were rapidly covered by a fibrous endothelial "cocoon" which virtually isolated them from the circulation

2 The asymptomatic foreign body which obstructs the main pulmonary artery causes severe changes in the lung and should be removed promptly, preferably within 48 hours after embolization if pulmonary function is to be significantly restored

3 Asymptomatic foreign body in a branch pulmonary artery produces much less general reaction of the lung than the main pulmonary arterial obstruction However, moderately severe microscopic changes were noted coming on immediately which tend to clear after a period of months, showing a relatively clear lung on x ray examination but with microscopic changes showing slight perivascular and peribronchial thickening and fibrosis

4 The first 2 weeks appear to be the most hazardous for uninfected sharp foreign bodies in pulmonary arteries After this time, there is little fear of erosion

5 Asymptomatic foreign bodies do not need to be removed from a branch pulmonary artery for fear of erosion once encystment has taken place However, these foreign bodies may be removed to improve pulmonary function if the vessel is large enough to anastomose or graft without subsequent thrombosis in this low pressure system

6 Lobectomy or segmentectomy is contraindicated for these lobes are viable and, since they are well aerated, are excellent pleural space fillers preventing overexpansion of adjacent lobes

7 The bronchial arteries have an important role in supplying blood to the lung distal to the foreign body Infarction in human beings may be due to differences in integrity of bronchial arteries

8. Anastomosis of a systemic artery to a pulmonary artery containing a foreign body causes so much pulmonary congestion, hemorrhage, and edema as to contraindicate this procedure.

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(For Discussion, see page 703.)

CAUSE OF DEATH IN CARDIOANGIOGRAPHY

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The intravenous administration of radiopaque agents is used clinically to delineate either the urinary tract or the heart and great vessels. Whereas the mortality of intravenous pyelography is reported[1] to be less than 1:150,000 that associated with cardioangiography is ten thousand times greater, or an appreciable 2 to 5 per cent.[2] This difference has been assumed to be a reflection of the greater risk associated with the patient having cardiac disease coupled with the fact that x-ray visualization of the heart requires an increased rate of injection as well as the use of a more concentrated organic iodide preparation. The purpose of the present investigation was to determine the mechanism responsible for these fatalities.

METHODS

General.—All experiments were carried out in adult mongrel dogs weighing between 10 and 20 Kg. The animals were anesthetized with pentobarbital sodium, 30 mg. per kilogram supplemented with small doses of succinylcholine. Artificial respiration was provided with a positive pressure ventilator connected to a tracheal cannula. Intravascular pressures were measured with Statham transducers and recorded on a Sanborn Poly-Viso recorder. Heparin (2 mg. per kilogram) was administered for anticoagulation. Donor blood used in the perfusion experiments was collected into plastic beakers containing enough heparin to produce a final concentration of 5 mg. per 100 ml. of blood.

Open Chest Animals.—The chest was opened through the left fifth interspace. Polyethylene catheters were placed in (a) the main pulmonary artery, (b) the left atrium, (c) the aorta through the femoral artery, and (d) the inferior vena cava from the femoral vein. Injections were made rapidly through a No. 10 Fr. catheter placed into the vena cava through either the femoral or jugular veins. The majority of the solutions administered consisted, because of their current favor, of commercially available 50 to 90 per cent diatrizoate salts of sodium and methylglucamine (Hypaque and Renografin). The remaining studies were carried out using 80 per cent NaI, 70

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to 75 per cent preparations of iodopyracet (Diodrast), iodomethamate (Neo-iopax) and acetrizoate (Urokon), and finally 40 per cent methiodal sodium (Skiodan). Isotonic saline and dilute solutions (30 to 35 per cent) of the various radiopaque agents were used as controls.

Isolated Perfused Lung.—The chest of the animal from which the lung was to be obtained was opened under artificial respiration by splitting the sternum longitudinally. The azygos vein and vena cava were ligated after heparinization and the heart, lungs, and aorta were removed without interrupting ventilation. The plastic cannula which had been filled to its tip with perfusion fluid was inserted through the outflow tract of the right ventricle and tied into the main pulmonary artery. Care was taken to keep air out of the pulmonary circulation. The pericardium, both ventricles, and the right atrium were dissected off and the left atrium drained at near zero pressure. The lung was suspended in a perforated plastic plate and venous drainage was collected in a plastic funnel and recirculated with a Sigmamotor pump. Perfusion was begun after an interruption of less than 2 minutes. The perfusion rate remained constant and was determined by increasing the arterial pump to the highest flow consistent with normal pulmonary arterial pressures monitored through a needle-tip catheter. Oxygenation was maintained by ventilating the lung throughout the experiments. Injections were made proximal to the arterial pump. Perfusates consisted of either whole blood, red cell mixtures, plasma, serum, or dextran-Ringer's solution. If blood was not to be used initially the lung was first flushed with large volumes of saline and dextran. Thoroughness of the rinsing was gauged by the whiteness of the lung surface and the clarity of the solution emerging from the venous drainage.

Total Body Perfusion.—Total body perfusion was carried out by previously described techniques.[3] The blood pressure response to radiopaque agents was determined under conditions of constant flow to quantitate the change in total peripheral resistance.

RESULTS

Intact Animal.—A total of 44 injections was made in 16 dogs. Respiratory alterations were prominent but will not be considered further at this time. The vascular response to these agents was variable. Marked reactions occurred either with heavier animals in which the absolute volume administered was greater, or when osmotically more concentrated materials were used regardless of chemical identity. A striking bradycardia with evidence of intracardiac block was frequently noted. Pulmonary edema, arterial desaturation, and signs of congestive failure appeared after repeated injections. The blood pressure always fell in response to these agents. Three distinctive patterns of decline, essentially unaffected by vagotomy, could be elicited in spite of some overlap.

1. *Monophasic hypotension with or without death of the animal:* The animals died in half of the 16 instances when 1 ml. per kilogram of sodium iodide,

iodomethamate, or methiodal sodium was injected (Fig 1) A similar result was obtained in 4 out of 6 cases with 3 ml per kilogram dosages of 90 per cent diatrizoates (Fig 2) Characteristically, as shown in Figs 1 and 2, the blood pressure fell precipitously and never recovered, pulmonary artery pressure increased strikingly while left atrial pressure fell, central venous pressure rose with vigorous pulsations, and the heart continued to beat for some time Inspections showed the left ventricle to be collapsed A similar response with eventual recovery was seen in the remaining studies with sodium iodide, iodomethamate, methiodal sodium, and high dosages of diatrizoates

2 *Diphasic hypotensive response* This type of reaction occurred frequently after injection of 1 ml per kilogram of 90 per cent diatrizoate (12 of 18), 70 per cent acetrizoate (3 of 5) and 75 per cent iodopyracet (3 of 4) (Fig 3) A milder variant was encountered with a similar dosage of 70 per cent diatrizoate (2 of 7) Initially there was a decline in blood pressure identical to that described above with bradycardia, occasional missed beats, and a decrease in pulse pressure However the arterial pressure rapidly recovered, with resolution of the pulmonary hypertension and an overshoot in left atrial pressure A more prolonged hypotension then ensued, with tachycardia, increased pulse pressure and a loss of the dicrotic notch in the pressure tracing A concurrent secondary rise and fall in pulmonary arterial and vena caval pressures were also noted It should be pointed out that the early pulmonary hypertension was frequently accompanied by similar changes in the pulmonary vein despite normal left atrial readings

3 *Paradoxical reaction* The remainder of the 1 ml per kilogram injections of radiopaque agents, including all solutions examined with 50 per cent or lesser concentrations, showed a paradoxical response (Fig 4) in that the typical delayed systemic hypotension was preceded by a hypertensive phase Initial pulmonary hypertension was never seen Sometimes in the early period a dip in blood pressure occurred that resembled the diphasic reaction in the presence of bradycardia and missed beats

Isolated Perfused Lung—Sixteen lungs were perfused Flow rates were below normal varying from 44 to 110 ml per kilogram per minute Mean pulmonary artery pressures were physiologic however, ranging from 5 to 25 mm Hg, the lower figures being obtained with plasma perfusates The degree of ventilation had no effect on the findings

In most cases the lung was first perfused with a colloid solution, subsequently blood or various red cell suspensions were used Radiopaque agents, including 80 per cent NaI in doses of up to 1 ml per kilogram, never produced pulmonary hypertension in the absence of red cells in the perfusate In fact, pulmonary vascular resistance generally fell under these conditions except when viscous diatrizoate solutions were injected In contrast, a phasic increase in pulmonary arterial pressure was almost uniformly seen when similar amounts were introduced into circulating blood or red cell suspensions (Fig 5) NaI, methiodal, and iodomethamate solutions gave such violent reactions that only acetrizoate, and diatrizoate solutions required almost the full dosage of 1 ml. per kilogram to double pulmonary artery pressure. The degree of response was in general proportional to the osmotic activity of the preparation tested. A positive response was never seen with 30 to 35 per cent concentrations. Microscopic examination of small blood vessels in the lung during a reaction

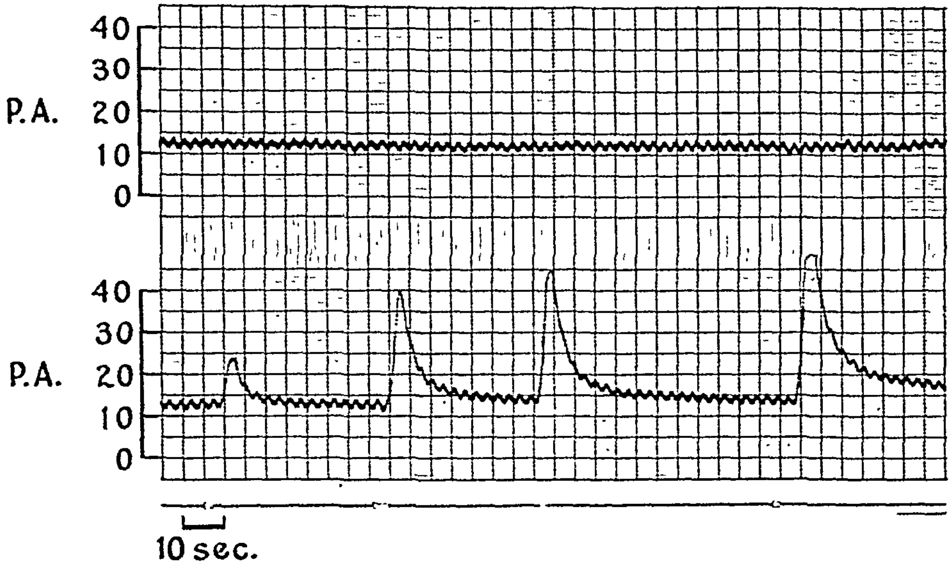

Fig. 5.—Effect of 1 ml./Kg. of 70 per cent Urokon, 90 per cent Hypaque, 70 per cent Diodrast, and 40 per cent Skiodan, respectively, on pulmonary artery pressure in the isolated lung perfused at a constant flow, first with plasma and then blood (below). The phasic increase in pulmonary vascular resistance is completely dependent upon the presence of red cells in the perfusate and is transitory in spite of recirculation.

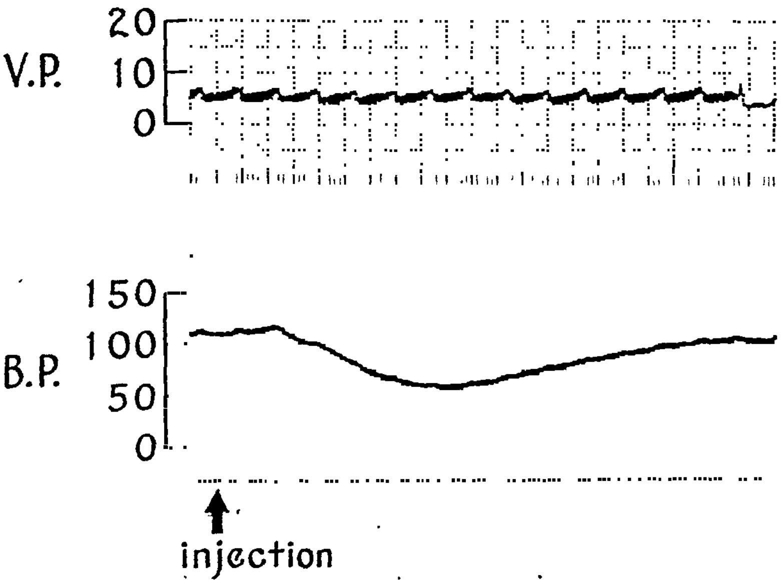

Fig. 6.—Effect of the intra-arterial administration of 1 ml./Kg. of 90 per cent Hypaque in the totally perfused dog. Note fall in arterial pressure at constant flow without change in venous pressure indicating an over-all decline in peripheral resistance. The flow in the aorta under these conditions is turbulent and red cell agglutination does not play as significant a role as seen after intravenous injection (Fig. 3).

showed red cell agglutination, plugging of arterioles and venules, and plasma skimming. Vasoconstriction was never observed. Instead, an average increase of about 20 per cent in vascular diameters occurred with re-establishment of blood flow. Permanent sections showed vascular congestion, pulmonary edema, red cell sickling, diapedesis, and clumping. A similar appearance has previously been reported in the intact animal.[4] The experiments were terminated after multiple reactions had been obtained because of the development of massive pulmonary edema.

Total Body Perfusion.—All of the agents used, ranging from 30 to 90 per cent in concentration, produced a fall in blood pressure at constant flow (Fig. 6). No effect was seen with isotonic saline. Various injections were made in 5 experiments.

COMMENT

Dotter and Steinberg reported in 1949 that cardioangiography had been performed in over thousand cases without fatality. They (and others) believed that this procedure was both simple and giving rise only to a sensation of warmth with occasional mild respiratory symptoms. Recently, perhaps because of more liberal dosages, disturbing side effects have been reported. These have included vascular collapse,[5] electrocardiographic abnormalities,[9-11] pulmonary edema, cyanosis,[13] and death.[14] Increasing awareness of this hazard has to a certain extent dampened the original enthusiasm for the procedure.

Vasomotor reactions to radiopaque agents have been recognized for some time in the experimental animal. Between 193 and 1935, five different groups[15-19] of investigators demonstrated the hypotensive potentialities of these solutions and suggested that both central and peripheral actions were involved. Weatherall, in 194, considered vasodilatation to be the primary mechanism. However, Gordon and his associates,[1] in 1950, described a "Diodrast reaction" in the dog which included bradycardia, cardiac irregularities, and a rise in central venous pressure. These findings have been confirmed by other workers.[illegible] Rowe and associates, in 1956, were the first to mention the occurrence of pulmonary hypertension. They observed this response in both the experimental animal and a patient who later died.

The present study demonstrates unequivocally that radiopaque preparations lower peripheral resistance. This finding, combined with the previously described pulse pressure, pulse wave, plethysmographic, skin temperature, and microscopic changes, confirms the vasodilator nature of these compounds shared with other hypertonic solutions.[7] This effect is delayed after intravenous injection because it depends upon direct contact with the peripheral vasculature. The elevation in pulmonary artery pressure, venous pressure, and heart rate seen at this time suggests a compensatory adrenergic release. This relatively benign peripheral phenomenon, perhaps of importance only in hypertensive and arteriosclerotic disease, is prece of a much more dangerous action gh th

Pressure data in Figs. 1 and 2 indicate that all of the dogs who succumbed did so of acute cor pulmonale. Circumstantial evidence obtained from case reports on patients who died suggests a similar cause of death, the respiratory system being vulnerable.[27] Almost all of the fatalities were in individuals known to be suffering from some type of central or peripheral pulmonary vascular stenosis.[28] Cyanosis, dyspnea, and signs of pulmonary congestion were noticeable at death. Pulmonary infarction, edema, and hemorrhage were prominent autopsy findings.

These experiments also provide information regarding the mechanism responsible for the increase in pulmonary vascular resistance. The studies in the whole animal show that the site of obstruction to blood flow through the lungs may be proximal or distal to the capillary bed. This phenomenon persists in the isolated preparation demonstrating that the central nervous system is unnecessary for its development. Its transitory nature in spite of recirculation is against an indirect effect mediated through the release of vasoactive materials. However, a direct action on the pulmonary vasculature is also ruled out because no response is elicited when red cells are absent from the perfusate. To be consistent with these observations any theory regarding the pulmonary vascular effects would have to assume that radiopaque agents increase the viscosity of the blood passing through the lungs by affecting its red cell component. The hypothesis is confirmed by the microscopic demonstration of red cell agglutination with plugging of vascular channels throughout the pulmonary parenchyma. This potential for altering the stability of the red cell stream is shared with other concentrated salt[29] and sugar solutions but not by urea which is unable to exert an osmotic differential across the red cell membrane.

On the basis of unpublished observations,[30] it appears that markedly hypertonic solutions, when given intravenously, immediately penetrate the red cells. These hypertonic erythrocytes become damaged and hemolyzed after passage through the circulation when they are re-exposed to a normal environment. Red cell agglutination is the first stage of this paradoxical hypotonic hemolysis.[31] The present studies show that doses up to 1 ml. per kilogram give rise to detectable changes in blood viscosity only when the osmotic activity of the solution is greater than 1,500 mOsm. per liter. Larger volumes tend to lower this threshold. The central effect requires a much stronger solution than the vasodilatation seen in the peripheral vasculature. This is well demonstrated by the paradoxical response elicited by relatively dilute radiopaque agents. Here, pulmonary hypertension is absent allowing the previously masked effects of hypervolemia and Bezold or direct cardiac excitation to develop before the later systemic hypotension.

A number of investigators have noted an association between the osmotic activity of angiographic media and their toxicity.[17, 20, 23, 24] Cotrim,[32] in 1955, clearly demonstrated this relationship but, in the absence of pulmonary vascular measurements, attributed death to primary cardiac depression. Most toxicity studies have been performed in small animals using relatively slow rates of injection. The lethal dose under these conditions is 4 or 5 times greater

TABLE I. OSMOTIC CONCENTRATION OF RADIOPAQUE PREPARATIONS

SOLUTION	OSMOTIC ACTIVITY (mOsm./L.)	RATIO TO PLASMA (330 mOsm./L.)
30% Urokon	950	3
35% Diodrast	1,100	3-4
50% Miokon	1,395	4-5
50% Hypaque	1,490	4-5
76% Renografin	1,730	5-6
70% Urokon	2,300	7-8
70% Diodrast	2,320	7-8
90% Hypaque	2,330	7-8
40% Skiodan	3,100	9-10
75% Neo-iopax	4,100	12-13

than that described at this time and chemical constituency appears to be more important.[33] Anaphylaxis continues to be mentioned as the cause of death in cardioangiography despite the fact that preliminary negative sensitivity tests are the rule.[34]

The phenomenon of red cell agglutination explains a number of hitherto poorly understood clinical observations. Complications have increased sixfold since 35 per cent solutions (originally developed for intravenous urography) have been replaced by 70 per cent preparations.[35] The newer less toxic radiopaque agents tend to have a lower osmotic activity because of their larger molecular size, poorer dissociation, and the replacement of inorganic by organic cations. The group of patients in which cardioangiography is known to have the greatest risk is that exemplified by the Eisenmenger syndrome. Here red cell agglutination is accentuated by polycythemia while the already damaged lungs are obviously more susceptible to vascular blockage. An increase in pulmonary vascular resistance is especially dangerous in this situation because systemic resistance is simultaneously lowered by the peripheral vasodilatory effects and the two circulations are connected by a right to left shunt.

In conclusion, it should be pointed out that the risk of agglutination could be markedly reduced, if not eliminated, by changes in the characteristics of the more concentrated radiopaque preparations. An attempt should be made to limit their osmotic activity to less than 1,500 mOsm. per liter by either decreasing their solubility or increasing their molecular size. A more difficult line of approach would be the development of solutions whose permeability, like urea, is so great that they are unable to develop an osmotic differential across the red cell membrane.

SUMMARY

One to 3 ml. per kilogram dosages of various concentrated radiopaque agents have been rapidly injected into the venous system of 24 dogs. A late peripheral vasodilatation was routinely observed. Solutions having an osmotic activity greater than 1,500 mOsm. per liter generally produced an initial pulmonary hypertension which sometimes resulted in death from acute cor pulmonale. Studies in the isolated perfused lung showed that the increase in

pulmonary vascular resistance was related to the presence of red cells in the perfusate. Microscopic observations demonstrated that these commercial preparations can cause red cell agglutination which is responsible for the pulmonary effects. The significance of these findings has been discussed in relation to clinical experience.

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(For Discussion, see page 703.)

PHYSIOLOGIC RESPONSE OF THE CORONARY CIRCULATION TO UNILATERAL PULMONARY ARTERY LIGATION

I. Initial Experimental Study

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A SIMPLE operative procedure capable of increasing the extracardiac collateral circulation to the coronary arteries deserves evaluation. Previous studies of the bronchial artery circulation impressed us with the increase in extracardiac collateral coronary blood flow which follows unilateral pulmonary artery ligation.[1, 2, 3]

Small extracardiac communications are normally present between the systemic circulation and the coronary arteries, but the flow through these vessels is of little significance in the normal dog. After chronic unilateral pulmonary artery ligation, these small communications become greatly dilated and are capable of carrying a large blood flow. The coronary arteries apparently contribute to the extensive collateral circulation of the lung after pulmonary artery occlusion. Under the experimental conditions outlined in this study (Fig. 1), these extracardiac collateral vessels may also carry a large volume of oxygenated blood into the coronary arteries. The purpose of this investigation is to determine the physiologic response of the isolated coronary vascular bed to a well-developed extracardiac collateral circulation. The anatomy of the extracardiac collateral coronary circulation has been accurately described for more than 50 years[4] but its physiologic significance is not generally appreciated. In recent years Gross,[5] Meek,[6] Hudson,[7] Kugel,[8] Gregg,[9, 10] Liebow,[11-11] Bloomer,[11, 12, 14] Vidone,[13] Glenn,[15] and their associates have contributed to our knowledge of this little understood but most significant collateral circulation.

A principal source of extracardiac collateral blood flow to the heart and lungs comes from the aorta through the bronchial arteries. Part of this systemic circulation is apparently shunted directly into the coronary vascular bed

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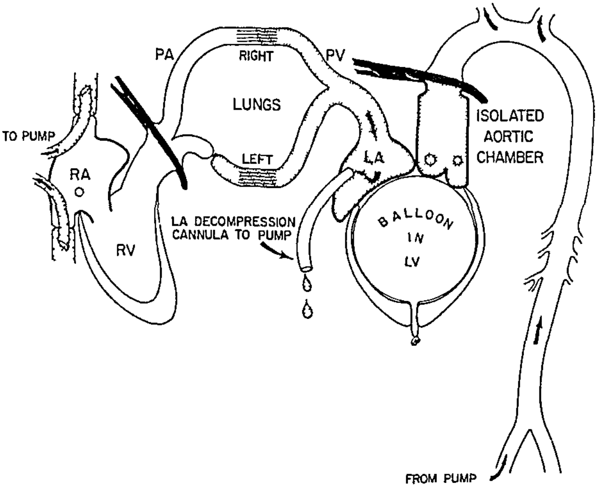

Fig 1—The experimental method which emphasizes the left auricular drainage, balloon occlusion of the left ventricle, and the creation of an "isolated aortic chamber"

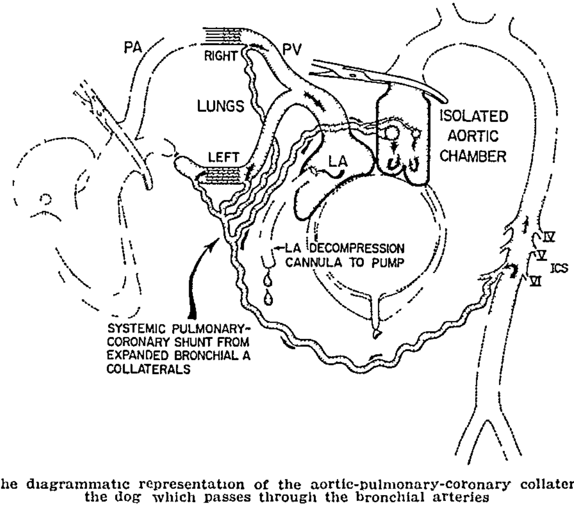

Fig 2—The diagrammatic representation of the aortic-pulmonary-coronary collateral flow, in the dog which passes through the bronchial arteries

while the remainder passes through the lungs and is returned to the left auricle (Fig. 2). In this experimental study we were able to investigate the systemic-coronary collateral circulation alone (Fig. 3). A direct measurement of the isolated extracardiac collateral blood flow to the coronary vascular bed, completely independent of the pulmonary venous-left auricular return, to our knowledge, has not been previously reported.

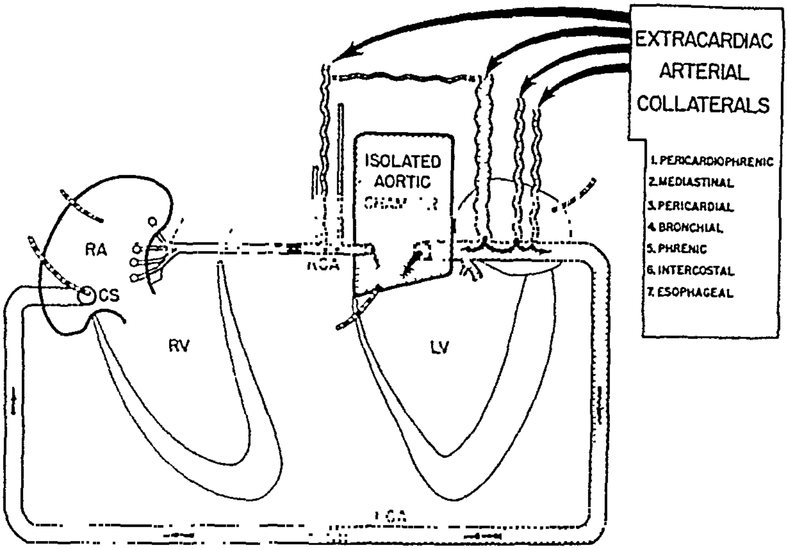

Fig. 3.—A diagram of the extracardiac sources from which arterial blood enters the isolated coronary vascular bed through auricular branches of the coronary arteries, under the conditions of the experimental method (after chronic unilateral pulmonary artery ligation). The retrograde flow into the "isolated aortic chamber" through the coronary ostia and the forward flow through the coronary vascular bed is demonstrated.

EXPERIMENTAL METHOD

Acute experiments were performed in 14 dogs (11 to 20 Kg.); 5 were control animals, and, in 9 dogs, the left pulmonary artery had been ligated from 3 to 19 months. Sodium pentobarbital anesthesia was used and a positive endotracheal pressure of 9 to 12 cm. H_2O was maintained by a mechanical respirator. Complete pump dependency was employed (disc oxygenator) and the aorta and pulmonary artery were clamped simultaneously within the pericardium. Either potassium citrate or anoxic cardiac arrest was utilized and the left auricle was immediately decompressed through a cannula which drained into the venous return to the pump. The coronary sinus, right auricle, ascending aorta (below the clamp), femoral artery and pulmonary artery were cannulated and pressures and flows recorded. The cardiac septa were intact. A balloon was inflated in the left ventricle of 10 animals (4 were controls) to prevent any remaining pulmonary venous flow from reaching the coronary ostia (Fig. 1). This created an "aortic chamber" which completely isolated the coronary ostia from all blood flow except that which came from extracardiac sources. Serial oxygen saturation determinations were made and continuous electrocardiographic tracings recorded. Repeated flows were measured from the cardiac cannulas with a graduate and timed for 30 seconds or longer. In several instances, a cannula was introduced into the left coronary ostia directly, through an aortotomy, to record the pressure and flow. At the completion of each experiment, plastic casts and angiograms were prepared of the collateral circulation to the heart and lungs by injecting 10 per cent radiopaque vinyl plastic into the doubly clamped descending thoracic aorta, containing only the bronchial and lower intercostal arteries. Temperatures varied during these experiments between 30° and 34.5° C.

This experimental method isolated the coronaries so that the extracardiac collateral circulation alone which perfused this vascular bed could be studied. The term, "high flow," will be used to designate the animals with chronic unilateral pulmonary artery ligation.

RESULTS

The results of this investigation were consistent in both the group with pulmonary artery ligation and in the controls. Only 5 of the 9 animals with an expanded collateral coronary circulation were studied with a balloon in the left ventricle. The remaining 4 dogs, however, showed the same response as the 5 reported, except that their coronary sinus return was greater without the compression effect of the inflated balloon. The coronary sinus flow was absent in the controls with a total coronary venous return of less than 1 ml. per minute. The group of animals with pulmonary artery ligation all showed more coronary venous flow than the controls and, in some instances, these flows were very high.

Studies previously reported and observations during this investigation impressed us with four important findings in dogs with chronic pulmonary artery ligation: (1) a prolonged sinus rhythm (up to 83 minutes) following pulmonary artery and aortic occlusion with the left auricle decompressed, (2) the inability to electively arrest the heart for more than a few minutes with potassium citrate, (3) the presence of 10 per cent vinyl plastic in the left coronary artery when the injection was made only into the doubly clamped descending thoracic aorta, and (4) a persistent flow of oxygenated blood into the right heart during cardiac arrest with pulmonary artery and aortic occlusion. These findings were entirely absent in the control animals.

In Fig. 4, the large volume of coronary venous return is recorded in an animal with ligation of the left pulmonary artery for 18 months. A volume of 135 ml. per minute passed through the isolated coronary vascular bed from extracardiac sources alone, when the left auricular drain was occluded, pulmonary vascular pressure rose with an increase in flow to 180 ml. per minute. After vasopressor stimulation, the flow was 360 ml. per minute and promptly fell to 8 ml. with Arfonad administration. These pharmacologic responses reflect the intimate relationship between this extracardiac collateral coronary flow and the systemic circulation.

The mean coronary sinus flow rates, expressed in terms of square meters of body surface (approximately 60 per cent of the coronary venous return[9]),

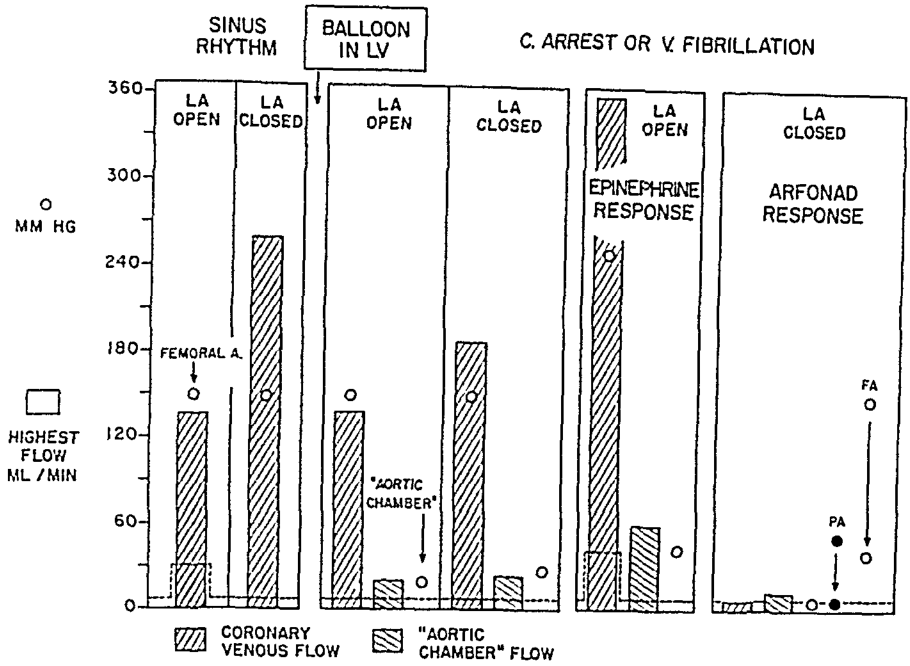

Fig. 1.—Dog 169. This graph demonstrates the high coronary venous flow which is present after prolonged unilateral pulmonary artery ligation (18 months). The pharmacologic response of the extracardiac collateral circulation to vasopressor and vasodilator drugs substantiates the *systemic arterial origin* of this collateral. The maximum response of the control group is represented by the broken line. Total cardiopulmonary bypass is present with aortic and pulmonary occlusion.

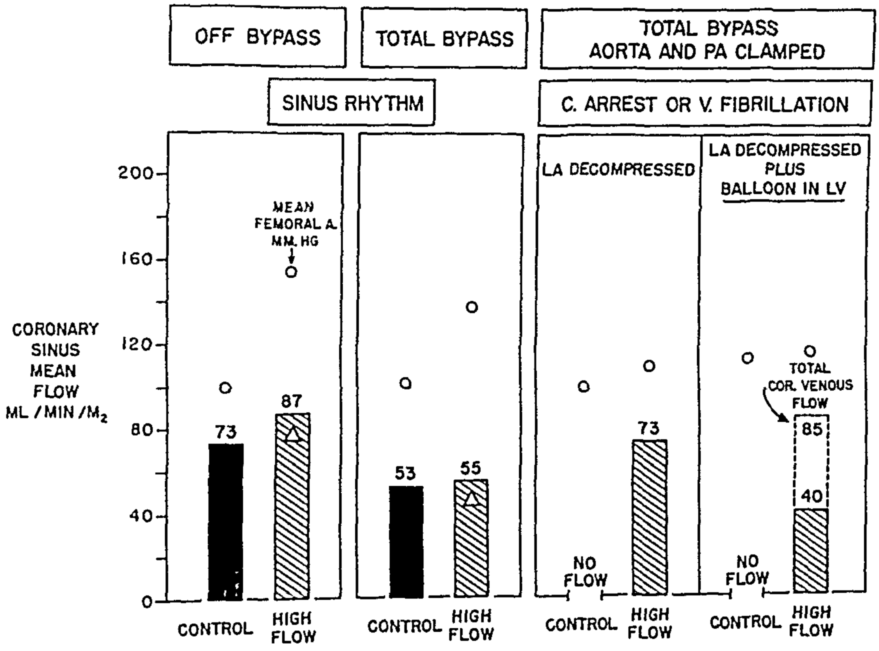

Fig. 5.—A graphic comparison of the mean coronary sinus flow (ml./min./M.²) in both groups of dogs (5 control—5 high flow dogs). The controls show *no coronary sinus flow* in the two boxes on the right, in contrast to the large flow present in the high flow group. (Δ—flow rates not recorded in 1 animal.)

in both groups of animals are compared in Fig 5 When the coronary vascular bed was completely isolated, there was no coronary sinus flow in the control group, but the animals with a high extracardiac collateral flow showed a mean volume of 40 ml per minute which passed through the coronary sinus There was a fall in flow in the ligated pulmonary artery group from 73 to 40 ml per minute after inflating the left ventricular balloon, this presumably represented an interference with coronary artery filling However, during this fall the total mean coronary venous return was 85 ml per minute, even though there was a complete absence of normal coronary blood flow, and represented the flow from extracardiac collateral communications into the coronary vascular bed This extracardiac collateral flow was equal to the coronary sinus flow in the normal beating heart with the animal off the pump

Studies of the "isolated aortic chamber" showed a pressure of 5 to 7 mm Hg with an absence of flow in the controls The high flow group demonstrated a mean pressure of 19 mm Hg and a flow of 29 ml per minute with oxygen saturations of 90 per cent (Fig 6) There was no flow in the control group and oxygen saturations could not be determined

The mean pulmonary venous flow into the left auricle during these experiments was 274 ml /min /M ^{2} in the high flow group and 23 ml /min /M ^{2} in the controls

The 10 per cent radiopaque plastic did not enter the extracardiac collateral coronary circulation in the control animals but was present in the animals with pulmonary artery ligation

DISCUSSION

This study emphasizes the marked difference between the meager extracardiac collateral coronary artery flow normally present and the very high collateral flow which results after prolonged unilateral pulmonary artery ligation, in the experimental animal A period of 5 months or more seems to be required following pulmonary artery occlusion to establish well developed collaterals between the systemic coronary circulation

Liebow, Bloomer, and their associates[14] have indirectly measured the collateral flow to the coronaries in the intact, living animal, employing dye dilution techniques, after cardiopneumopexy and pulmonary artery ligation They concluded that the collateral blood flow entering the coronary sinus was 4 to 16 per cent[14] of the total coronary sinus flow, in the absence of myocardial ischemia, and suggested the possibility of ligating a lobar pulmonary artery in patients with "coronary insufficiency"

The dog's heart is left coronary preponderant, in contrast to the human heart, however, it is of interest that Louis Gross,[2] in his classical monograph published in 1921, described the coronary blood supply in *100 human hearts* and demonstrated a shift from a right or balanced coronary heart to left coronary preponderance during the *fourth* to the *eighth* decades of life

The clinical application of this experimental study to human patients is speculative at this time Further investigations are now in progress in an effort to clarify certain physiologic aspects of this simple operative procedure, unilateral ligation of the pulmonary artery.

SUMMARY

A comparison of the results in the control animals and high flow dogs with unilateral pulmonary artery ligation is shown in Fig. 6.

		CONTROLS	HIGH FLOW
WELL EXPANDED EXTRACARDIAC CORONARY A COLLATERALS		ABSENT	PRESENT WITHIN 5 to 12 MONTHS
CARDIAC ARREST	ANOXIC	ARREST WITHIN 15 MINUTES	SINUS RHYTHM FOR 23 to 83 MINUTES
	POTASSIUM	PROLONGED	SHORT DURATION
PLASTIC (10 %) STUDIES		NO CORONARY A. FILLING	LEFT CORONARY A. FILLS
BALLOON IN LV — L.A. OPEN			
CORONARY VENOUS FLOW (MEAN)		0.8 ML./MIN/M_2 (NO COR SINUS FLOW)	85 ML./MIN./M_2 (COR. SINUS FLOW-40)
"ISOLATED AORTIC CHAMBER" (MEAN)	PRESSURE	5 MM. HG	19 MM HG
	FLOW	NO FLOW	29 ML./MIN.
	O_2 SATURATION	NO FLOW	90 %
LEFT AURICULAR FLOW (MEAN)		23 ML /MIN /M_2	274 ML /MIN /M_2

Fig. 6.—A summary of the important differences in the physiologic response of the extracardiac collateral coronary circulation in the two groups of dogs.

CONCLUSIONS

Recognizing that these are experimental studies, performed in the bypassed heart under altered physiologic conditions, the results are nevertheless significant and demonstrate the potential extracardiac blood flow which is capable of entering an isolated coronary arterial bed, after the chronic ligation of one pulmonary artery. Further experimental and clinical investigation is necessary to determine the advisability of employing pulmonary artery ligation in patients with coronary artery disease.

We wish to express our appreciation to Mr. Boyd Perry, Mr. Thomas Perry, Mrs. Mary E. Garrard, and Mr. Eugene Varga for their technical assistance.

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DISCUSSION

(PAPERS BY WRIGHT [PAGE 643], HARDY [PAGE 652], BRUNS [PAGE 662], BREWER [PAGE 670], READ [PAGE 685], LITTLEFIELD [PAGE 696], AND THEIR ASSOCIATES)

DR WILLIAM E. BLOOMER, New Haven, Conn —It is a pleasure to discuss this very nice presentation by Dr. Littlefield Working with Drs Lindskog and Liebow, we became interested in the potential of the bronchial arterial supply after ligation of the unilateral pulmonary artery back in 1947

This slide, I think, shows the extent to which bronchial arteries can increase in size on one side. You can see on this side, where there is no red injection, there is a lack of pulmonary arteries, and these black vessels represent the increased bronchial arterial supply on that side. This made us wonder if the potential of bronchial arteries might be applied to the coronaries in the old cardiopneumonopexy that was suggested and done by Lezius

[Slide] In using this technique, we felt that this might supply arterialized blood to the lung and, by way of newly formed vessels across the transpleural plane, to the myocardium.

In this slide, one can see, in such an injection corrosion specimen, newly formed vessels going from the coronary arteries into the pulmonary vessels, where the coronaries have been injected in red

[Slide] This is also seen in this specimen, and here you see the pulmonary arteries have also been filled by way of the bronchial arteries when the aorta was injected in black, and the red and the black mix together here in the lingula where this has been applied to the heart.

I would like also to point out that not only is there a potential supply of blood by way of the bronchial arteries into an ischemic myocardium, but also this lung may form a bridging effect from one ischemic area of the heart to another, and we think this may be important.

[Slide] Not only were these transpleural vessels shown but, also, this very important, we think, retrocardiac plexus, which has been emphasized by Dr. Littlefield this morning. These vessels, injected in red here, represent connections between the bronchial arteries and the anterior and posterior left atrial arteries that arise from the left circumflex.

[Slide] Diagrammatically, then, it seems that the bronchial arteries, after ligation of the pulmonary artery, and having already preformed small connections between the coronary artery here, become greatly enlarged, and the same mouths that feed the bronchial arteries feed these retrocardiac vessels, which also feed the coronary arteries, and it seems that they do form a very important collateral flow.

I would like to emphasize that, as shown by Stern and Liebow's findings, one doesn't have to tie off the whole pulmonary artery; the lingular artery works fine. I understand that, although we have only begun to evaluate this in patients, Dr. Burford has started to incorporate this principle in some of his poudrage procedures, and we will be very interested in seeing his results.

DR. CHARLES P. BAILEY, Philadelphia, Pa.—I was particularly interested in Dr. Richard Hardy's presentation of a new elastomer foam prosthetic for arterial replacement. We didn't have any of that material, but we did have similar problems. One of the problems that he did not particularly mention was the difficulty of containing blood within such a prosthetic graft when the patient was heparinized. We have had this problem not only in replacement of peripheral arteries but in replacement of parts of the aorta, as when we use part of the aortic wall to repair the aortic valve.

[Slide] Dr. Edward Fitch, of our resident staff, devised this particular prosthetic material. It consists of two slabs of compressed Ivalon sponge with an intervening sheet of Teflon mesh, both of which are readily available. The three layers of the "sandwich" are compressed and autoclaved. They end up as a single thickness sheet with good adhesion of its various components. One then has the strength of the Teflon and its durability, and at the same time the advantages of handling of Ivalon sponge.

This is the material before compression, and you can see the tremendous difference in the thickness of the slabs of Ivalon before and after compression. This is compressed 15 to 1. The usual compression of Ivalon for septal defect repair is about 6 to 1.

At this compression there is no leakage of blood through the prosthetic material nor through the stitch holes that are created in sewing it to the arterial wall.

[Slide] This prosthetic can be made in tubular form, the inner slab being rather thin, as it is wrapped around the inner mold. The Teflon is wrapped around and then a thicker slab of Ivalon is added. Of course when it comes out of the mold it has a flange on either side and you ought to really cut off the flange for esthetic purposes as well as for ease of handling.

[Slide] This material can be made in the form of a bifurcation graft just as well, if you wish.

Using this material, either to replace segments of aortic wall that have been removed or in the replacement of an entire artery, we have found no unexpected difficulty. It is tolerated well by the tissues. We were afraid at first that the fibrous tissues of healing might not grow into the material and cause it to be thoroughly incorporated, but this fear has proved to be unfounded. At least connective tissue fibrils must penetrate into the porosity of the prosthesis, because it attaches well to all contiguous structures. Neither in the experimental animals in which this was worked out nor in human beings has there been any difficulty. If you don't have any of this new elastomer foam material you can easily make up a homemade prosthesis which will work quite well.

DR. PAUL W. SANGER, Charlotte, N. C.—The monumental work that Dr. Holman reported to this Society when he was President about 5 years ago on post-stenotic dilatation, I think, shall ever remain a pattern for studying this complex phenomenon.

It is quite true that there is definitely a turbulence in the post stenotic dilatation area, but we have a different opinion as to the effect of this turbulence We believe another hydrodynamic phenomenon called cavitation plays the most important role in the development of post stenotic widening Cavitation was originally described as "the boiling of water in a tube at ordinary temperature" Liquids flowing through a closed system generally contain gases in equilibrium with the fluid When the pressure equilibrium becomes disturbed, there is a tendency for a cavity (bubble) formation. Under certain conditions, the sudden changes and alterations in velocity and pressure cause an alternate formation and collapse of gas bubbles The human blood is a supersaturated fluid of oxygen, CO_2, and nitrogen When there is a disturbance, innumerable small "micro explosions" are created The consequence of this long acting process is severe injury to the walls of the system in which the fluid is flowing

A long continued bombardment of these "micro explosions," we think [slide] results in destruction of the media of the artery Note the fractionation of the elastic tissue The bottom portion of this slide was taken from the same aorta just a few centimeters beneath the post stenotic dilatation You will see the normal histologic appearance of the artery

The second slide demonstrates cavitation produced in a glass model You will observe that just beyond the constricted portion of the tube are numerous gas bubbles We believe the implosion or explosion of these gas bubbles causes severe injury to the vessel walls

DR PAUL NEMIR, Jr, Philadelphia, Pa —I rise to congratulate Dr Hardy on his presentation Certainly this gives promise of at least getting us closer to the prosthetic, because it would seem to obviate that factor which, at least in our hands, troublesome at times, that of bleeding at the time of insertion of the prosthetic

We have used a number of different substances, such as homografts, heterografts, nylon, Teflon, and Ivalon in about 60 animals, implanting the material into the thoracic abdominal aorta As far as intimal replacement and fibroblastic proliferation are concerned there is very little difference with respect to the materials which we have used We have examined these animals after periods of as long as 12 to 13 months

It would seem that the major problem would be to obviate the factor of bleeding at the time of insertion and this certainly gives promise of doing that.

DR ROLLINS HANLON, St Louis, Mo —I would like to comment on the presentation of Dr Read

Some time ago we were interested in this problem of toxic factors in angiocardiography We studied it in some 40 dogs, injecting 70 per cent Urokon in three areas of the circulatory system—the jugular vein, the right ventricle, and the pulmonary artery

We found that the closer to the pulmonary parenchyma one injected the material, the greater was the incidence of deleterious reaction in the lung We noted severe agglutinative thromboses in the dog's lung (similar to those described by Dr Read) in about [illegible] per cent *of the instances in which we injected Urokon into the pulmonary artery* directly We then suggested that caution should be exercised in selective angiocardiography in man when injections are made close to the pulmonary substance

We therefore approached selective angiocardiography in patients with some caution However during the past 2 years I am happy to say that in something over 700 injections through an intracardiac catheter with 85 or 90 per cent Hypaque we have had no fatal or serious reactions These injections were done by Dr J Gerard Mudd in his cardiac catheterization laboratory and the negligible reaction rate is probably associated with the fact that most injections were made with the catheter tip in the outflow tract of the right ventricle or in the left atrium, and only infrequently and with carefully reduced dosage into the pulmonary artery directly Also, the contrast substance was not Urokon, as in our experimental studies.

DR. THOMAS C. MOORE, Indianapolis, Ind.—I, too, should like to comment upon the very interesting paper of Dr. Read.

We have been interested in studying the deleterious effects of intravascular radiopaque media in the laboratory at the Indiana University Medical Center and have carried out studies employing injection into the peripheral arteries of dogs. The response has been evaluated by means of the impedance plethysmograph. We found that dilute doses of radiopaque media tended to have a vasodilating effect, whereas concentrated doses had a very markedly constricting effect. However, with repeated large injections the vasoconstricting effect became progressively less in degree. We found, also, that repeated small injections tended to protect against the constricting effect of a subsequent larger injection.

In addition to these findings, we also discovered that a prior injection of procaine protected against this effect. This finding confirmed the observations of Dr. Keith Grimson with respect to injections into the renal arterial tree. It appears that the response to intravascular injection of radiopaque media may well be a constrictive one and probably not mediated through the sympathetic system.

Dr. Robert Shaw, of Boston, has shown clinically that this response occurs even in sympathectomized extremities. I think that the observations of Dr. Read may be quite helpful, indeed, in eliciting the actual mechanism of this response.

I should like to ask him if he has attempted to use repeated injections in his preparations, and whether he has attempted to use prior injections of procaine. It may well be that the response occurs as a result of some damaging effect of this medium on the red cells and that this vasoconstricting response may be actually secondary to red cell damage.

It also might be worth while to expose some blood to the media, to filter the red cells off and to see what the resulting plasma is able to do in the way of vasoconstriction. I think it is an exceedingly important and worth-while study.

Announcements

THE AMERICAN ASSOCIATION FOR THORACIC SURGERY

Notice of Annual Meeting

The Fortieth Annual Meeting of The American Association for Thoracic Surgery will be held May 11, 12, and 13, 1960, in Miami Beach, Florida. Headquarters will be the Deauville Hotel.

Requests for Hotel Reservations

These should be mailed directly to Mrs. Mildred Sander, Reservation Manager, Deauville Hotel, Miami Beach, Florida. Please mention this Association, the type of accommodation desired, the date, and approximate hour of arrival and departure. If accommodations are desired elsewhere please communicate directly with the hotel of your choice.

Material for the Program

SCIENTIFIC PAPERS.—Abstracts of all papers proposed for presentation at the 1960 meeting *must be received on or before* **November 15, 1959,** otherwise they will not be considered by the Program Committee. These should be labeled "For Thoracic Surgery Forum" or "For Regular Program" depending upon the nature of the subject matter, in the same manner as in previous years. They should contain from 200 to 250 words that accurately reflect the content of the completed paper.

Six, repeat, six clearly legible copies of *each* abstract must be sent to Miss Ada Hanvey, Administrative Assistant, The American Association for Thoracic Surgery, 308 Carondelet Building, 7730 Carondelet Avenue, St. Louis 5, Missouri.

Essayists selected for the program are reminded that papers presented at the meeting *must* be handed to the secretary *immediately* after their presentation. If they are not ready at that time there is a chance that they will not be published in THE JOURNAL OF THORACIC AND CARDIOVASCULAR SURGERY.

Applications for Membership

Applications for Associate Membership in the Association must be received by the Membership Committee *not later than* **November 15, 1959,** otherwise the application will be deferred for consideration until the 1961 meeting.

Applicants must be sponsored by three Active or Senior Members of the Association. In addition to the signature on the application form, the sponsors will forward a *separate* letter concerning the applicant directly to:

Frank Gerbode, M.D.
Chairman of the Membership Committee
Stanford University Hospital
San Francisco 15, California

Sponsors are reminded that *new* letters of recommendation must be forwarded to the Chairman of the Membership Committee should their applicants be held over for reconsideration a *second year.*

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Original Communications

THE SURGICAL TREATMENT OF CYLINDROMA (ADENOID CYSTIC CARCINOMA) AND MUCO-EPIDERMOID TUMORS OF THE BRONCHUS

W. Spencer Payne, M.D. (by invitation), F. Henry Ellis, Jr., M.D.,** Lewis B. Woolner, M.D.*** (by invitation), and Herman J. Moersch, M.D.,**** Rochester, Minn.*

THE CLASSIFICATION of primary cancer of the lung now in use at the Mayo Clinic includes a group of malignant tumors that originate in the mucous glands (Table I). The term "bronchial adenoma" is customarily used when discussing this group of tumors, which includes the carcinoid, the cylindroma, and the muco-epidermoid tumor. The term "adenoma," however, has a benign connotation which does not accurately describe the clinical behavior of many of these tumors.

The clinical features and the malignant potentialities of the carcinoid tumor have been the subject of many publications from this[1-3] and other institutions[1-8] and will not be discussed further. The present study is concerned primarily with the other two tumors of this group, the cylindroma (adenoid cystic carcinoma) and the muco-epidermoid tumor of the bronchus.

From the Mayo Clinic and Mayo Foundation, Rochester, Minn. The Mayo Foundation is a part of the Graduate School of the University of Minnesota.

Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery, Los Angeles, Calif., April 21-23, 1959.

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HISTORICAL REVIEW

Heschl[9] in 1877 made the first report on cylindroma of the bronchus, and Müller[10] in 1882 was the first to describe what is now classified as a carcinoid tumor of the lung. In spite of the early recognition of these two types of tumor, their significance was not generally appreciated for many years. In the early 1930's, Kramer,[11] Geipel,[12] and Wessler and Rabin[13] distinguished a group of tumors called "adenomas" from the more common and more malignant bronchogenic carcinomas. In 1937, Hamperl[14] clearly distinguished the cylindroma from the carcinoid tumors within this "adenoma" group.

TABLE I. CLASSIFICATION OF PRIMARY CANCER OF THE LUNG

- I. Tumors of bronchial epithelial origin
  - A. Bronchogenic carcinoma
    - 1. Squamous cell carcinoma
    - 2. Adenocarcinoma
    - 3. Large cell carcinoma
    - 4. Small cell carcinoma
  - B. Alveolar cell carcinoma (terminal bronchiolar)
- II. Tumors of mucous gland origin ("bronchial adenoma")
  - A. Carcinoid tumor
  - B. Cylindroma (adenoid cystic carcinoma)
  - C. Muco-epidermoid tumor
- III. Tumors of mesenchymal origin
  - A. Lymphosarcoma
  - B. Fibrosarcoma

The term "cylindroma" was originated by Billroth[15] in 1859 to describe an orbital tumor. The term was subsequently used to describe the histologic appearance of certain tumors arising in the lacrimal and salivary glands and in the glandular structures of the breast and mucous membranes of the mouth, nose, paranasal sinuses, larynx, trachea, and bronchi.[16] The term "adenoid cystic carcinoma" is of more recent origin[17] and is used as a synonym for cylindroma as it accurately connotes the malignant nature and microscopic appearance of these tumors.

Muco-epidermoid tumors of the bronchus were first described by Liebow[5] and, as he has pointed out, they are identical histologically with the muco-epidermoid tumors originating in the salivary gland which Stewart, Foote, and Becker[18] described. In the past, these tumors have been provisionally classified by both Liebow[5] and us as cylindromas. Tumors of the muco-epidermoid type are included in the present discussion, not because they represent a histologic variant of cylindroma, but because this study of these lesions has led us to believe that they represent a distinct and separate clinical and pathologic entity which should not be confused with adenoid cystic carcinoma.

The chief histologic feature of adenoid cystic carcinoma (Fig. 1, *a*) is the arrangement of small, darkly staining cells in anastomosing solid or cystic cords. Between these collections of tumor cells are irregular areas of relatively acellular connective tissue which impart a "Swiss cheese" pattern.

The main feature of the muco-epidermoid tumors (Fig. 1, *b*) is the histologic pattern of an intimate admixture of well-differentiated mucous cells and benign-appearing squamous elements, the cells of which may show intercellular bridges.

SCOPE OF PRESENT STUDY

In the present study we reviewed all the available clinical and pathologic material of all patients given a diagnosis of adenoma of the lower part of the respiratory tract at the Mayo Clinic in the 32-year period, 1927 through 1958. All tumors arising primarily in the trachea were excluded, but primary bronchial tumors showing tracheal involvement by direct extension were included. Also excluded from study were metastatic tumors to the lung.

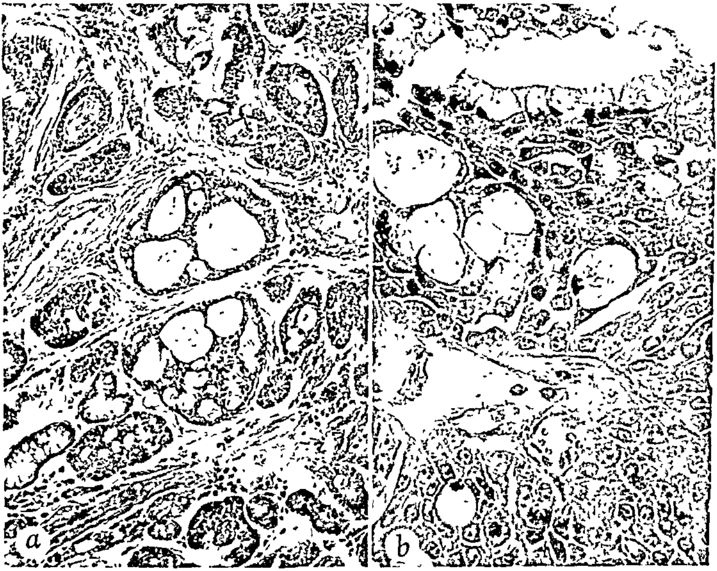


Fig. 1.—Sections showing the main histologic features. *a*, Adenoid cystic carcinoma (hematoxylin and eosin, ×130). *b*, Muco-epidermoid tumor (hematoxylin and eosin; ×400).

During this 32-year period, 162 so-called adenomas of the bronchus were encountered; 145 of these (89.5 per cent) were carcinoid tumors of the bronchus and will not be considered further; 13 (8.0 per cent) were adenoid cystic carcinomas of the bronchus, and 4 (2.5 per cent) were muco-epidermoid tumors (Table II).

Table II. Tumors of Mucous Gland Origin
("Bronchial Adenoma")

	CASES	PER CENT
Carcinoid tumors	145	89.5
Adenoid cystic carcinoma	13	8.0
Muco-epidermoid tumors	4	2.5
Total	162	

TABLE I. AND PATHOLOGIC DATA ON PATIENTS

CASE	AGE (YR.) AND SEX	SYMPTOMS (YR.)	SITE IN BRONCHUS	LE: . AT TIME OF TREATMENT				TREATMENT	RESULT
				EXTENSION		METASTASIS			
				MEDIASTINAL	TRACHEAL	NODAL	DISTANT		
				Cylindroma (Adenoid Cystic Carcinoma)					
1	42 F	1	R. main	+	+	?	?	Conservative	Died 2 yr. later; residual tumor
2	64 M	1	R. main	?	+	?	0	Conservative	Died 11 yr. later with metastases
3	36 M	1	L. main	0	+	0	0	Pneumonectomy (palliative)	Died 4 yr. later of metastasis (?)
4	50 M	6	R. lower lobe	+	+	+	0	Conservative; not resectable at exploration	Died 1 yr. later with metastasis
5	31 M	1½	L. main	?	+	?	?	Conservative	Died 9 mo. later; residual tumor
6	39 F	1½	L. main	0	0	+	0	Pneumonectomy	Alive 12¾ yr.; probable cure
7	48 M	15	R. lower lobe	0	0	0	0	Pneumonectomy	Died 10 mo. after operation of bronchopleural fistula; no residual tumor
8	60 F	¼	R. main	?	0	?	+	Conservative	Died 2 yr. later with metastasis
9	52 F	1	L. main	0	+	+	0	Conservative	Died 1 wk. after treatment; residual tumor
10	46 F	1½	R. main	+	+	+	0	Pneumonectomy (palliative)	Alive 4½ yr.; residual tumor
11	31 F	1	R. lower lobe	0	0	0	0	Right middle and lower lobectomy elsewhere	Dead 8 yr. later of widespread metastasis
12	45 F	4	L. lower lobe	+	+	+	0	Pneumonectomy (palliative)	Alive 2½ yr.; residual tumor
13	45 M	1	R. main	0	+	+	0	Pneumonectomy (palliative)	Alive 1 yr.; residual tumor
				Muco-Epidermoid Tumors					
14	65 M	6	R. main	0	0	0	0	Conservative	Died 2 wk. later; tumor present
15	44 M	⅙	R. upper lobe	0	0	0	0	Conservative	Died 4 yr. later; tumor present
16	47 F	3	L. main	0	0	0	0	Pneumonectomy	Alive 10 yr.; probable

CLINICAL REVIEW OF CASES

Age and Sex—The ages of the 13 patients with adenoid cystic carcinoma ranged from 31 to 65 years, with an average age of 45 years at the time of diagnosis Six patients were men and 7 were women (Table III)

The 4 patients with muco epidermoid tumors ranged in age from 44 to 65 years, averaging 50½ years They too showed no sex predilection All patients in this study were of the Caucasian race

Symptoms—The average duration of symptoms of patients with adenoid cystic carcinoma was 3 years at the time of diagnosis Although cough or wheeze was the most common symptom of long duration, usually some more recent and urgent symptom caused the patient to seek medical attention (Table IV) Only 1 patient (Case 8) was devoid of respiratory symptoms Her chief complaint was referable to a metastatic adenoid cystic carcinoma involving the optic chiasm and the pituitary The primary lesion in the lung was found incidental to routine thoracic roentgenography

The average duration of symptoms of patients with muco epidermoid tumors was about 3 years at the time of diagnosis All had primary pulmonary complaints, and none had evidence of metastasis (Table IV)

TABLE IV PRIMARY SYMPTOMS

	ADENOID CYSTIC CARCINOMA (13 CASES)	MUCO EPIDERMOID TUMORS (4 CASES)
Cough	12	4
Hemoptysis	8	3
Dyspnea	7	3
Pain in thorax	7	1
Wheeze	9	4
Chills and fever	6	4
Loss of weight	8	1
Symptoms referable to central nervous system	1	0

The symptoms of both groups of patients were mainly those of bronchial irritation, or bronchial obstruction and pneumonitis It was apparent that patients with muco epidermoid tumors were more often acutely ill with suppurative complications than were those with adenoid cystic carcinoma

Interestingly, none of the patients of either group had any clubbing of digits although evidence of chronic pulmonary suppuration was apparent None complained of arthritis, hoarseness, or symptoms of vasomotor instability suggestive of a functioning tumor

Roentgenographic Appearance—Roentgenographic examination of the thorax was of considerable importance in the study of these patients The original roentgenograms of approximately half of the patients were available for review those for 7 of the patients with adenoid cystic carcinoma and for 2 of those with muco-epidermoid tumors of the bronchus The descriptive reports of the roentgenologists only were available for the remaining 8 patients

The thoracic roentgenograms of 2 of the 13 patients with adenoid cystic carcinoma of the bronchus showed no abnormality at the time of diagnosis. The roentgenograms of 7 of the remaining 11 patients showed lobar collapse (Fig. 2, *a*), and those of 4, massive collapse of one entire lung similar to that seen in Fig. 2, *b*. In 3 of the patients with evidence of lobar collapse, a mass was also demonstrable roentgenographically.

The thoracic roentgenograms of all 4 of the patients with muco-epidermoid tumors showed abnormalities, and all manifested collapse of one entire lung (Fig. 2, *b*).

None of the thoracic roentgenograms taken at the time of diagnosis showed signs of cavitation, pleural fluid, obstructive emphysema, or involvement of bone. Furthermore, none of the roentgenograms studied presented signs sufficiently distinctive that one type of tumor could be differentiated from the other or from some other processes causing bronchial obstruction.

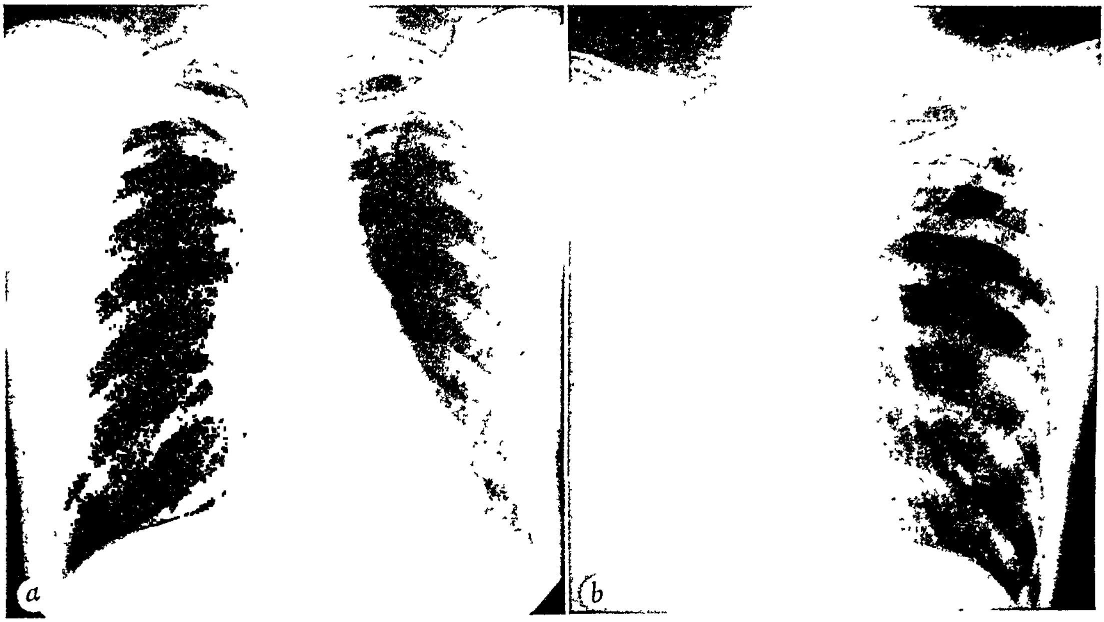


Fig. 2.—Thoracic roentgenograms *a*, Patient (Case 12) with adenoid cystic carcinoma showing collapse of left lower lobe of the lung. *b*, Patient (Case 14) with a muco-epidermoid tumor of the right main bronchus producing massive collapse of one entire lung.

Bronchoscopic Appearance.—Bronchoscopic examination had been performed on all of the patients in this study. All of the tumors arose from either a primary or secondary bronchus, and all but one could be seen at the time of bronchoscopic examination. Endoscopic biopsy was the chief means of establishing the histologic diagnosis, and adequate specimens were obtained for diagnosis from all tumors that could be visualized. Thus, the diagnosis was made for all 13 patients with adenoid cystic carcinoma by this means and for 3 of the 4 patients with muco-epidermoid tumors. The only patient in whom the tumor could be neither seen nor biopsied was a patient with an extrabronchial muco-epidermoid tumor which produced bronchial obstruction by external compression (Case 15).

Each type of tumor had a distinctive endoscopic appearance The adenoid cystic carcinomas of the bronchus presented as polypoid infiltrative tumors that partially or completely obstructed a bronchus Often the tumor was covered with necrotic material and bled easily on manipulation Grossly, they had the general appearance of bronchogenic carcinoma Four of the 13 patients with adenoid cystic carcinoma showed signs of gross carinal or tracheal involvement at the time of the initial endoscopic examination

The usual bronchoscopic description of muco epidermoid tumors was that of a large polypoid endobronchial mass that completely obstructed a primary bronchus, presented a smooth clean surface, and did not readily bleed on manipulation None of these tumors presented signs of infiltration or tracheal involvement The single tumor that could not be visualized had caused bronchial obstruction that appeared endoscopically to be due to external compression

Evidence of bronchial infection was present in all of the patients at the time of initial examination, but it was most marked in those with muco epidermoid tumors All 4 of these patients were described as having copious amounts of pus flowing from the region distal to the tumor, whereas only 1 of the patients with adenoid cystic carcinoma had such massive drainage at the time of initial bronchoscopic examination

Cytologic Studies—Cytologic studies were carried out on the sputum or bronchial secretion or both of 4 patients Two of these were patients with adenoid cystic carcinoma, and malignant cells were identified in the bronchial smears or secretions from each In 1 of these 2 patients, clumps of cells were identified which were suggestive of adenoid cystic carcinoma

Cytologic studies on the 2 patients with muco epidermoid tumors of the bronchus did not reveal any abnormal cells

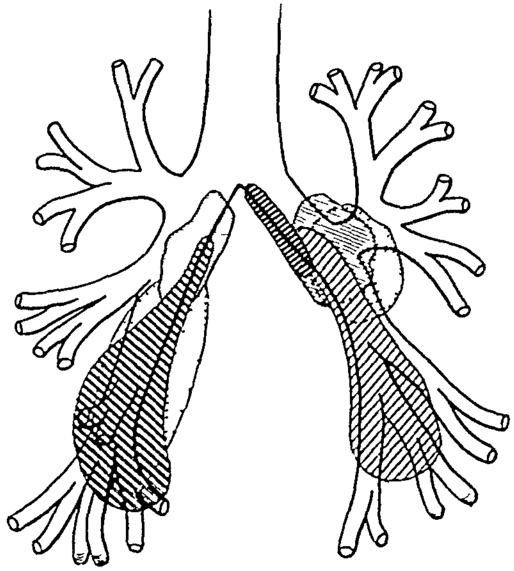
STUDY OF THE GROSS AND MICROSCOPIC PATHOLOGY

Information regarding the gross appearance and extent of spread of these tumors which will be presented in this portion of the paper was obtained from a review of gross surgical specimens available, the descriptive operative reports of surgeons in these cases, and from a review of pathologic data and material obtained at the time of necropsy Although microscopic sections were available in all 17 cases in this study, and were reviewed, additional sections were obtained for microscopic study when the gross specimens were available in order to document the characteristics of these tumors further We shall present here only the details concerning these additional microscopic studies Findings with regard to extension of the lesion at time of treatment are given in Table III They were derived from all sources then available and are more inclusive than those we shall now present

Adenoid Cystic Carcinoma—In 7 of the 13 cases of adenoid cystic carcinoma, the gross specimen of lung containing the primary tumor was available for review Six were surgical specimens and one was obtained at postmortem examination

The distribution and area of gross involvement of the tumor found in these seven specimens of lung is schematically illustrated in Fig. 3, *a*. All of these tumors involved major bronchi, and none presented as a peripheral pulmonary lesion. The typical gross appearance of the adenoid cystic carcinomas was that of an infiltrating malignant lesion (Fig. 4). The endobronchial surface of these tumors was nodular and polypoid and involved the bronchial wall in a tubular fashion. Over the ulcerating endobronchial surface, the tumors were covered with necrotic material. The walls of major bronchi were thickened and indurated. Two of the seven specimens showed gross involvement of the tracheobronchial junction. Pulmonary parenchymal involvement was not unusual,

CYLINDROMA (adenoid cystic carcinoma)



MUCOEPIDERMOID TUMOR

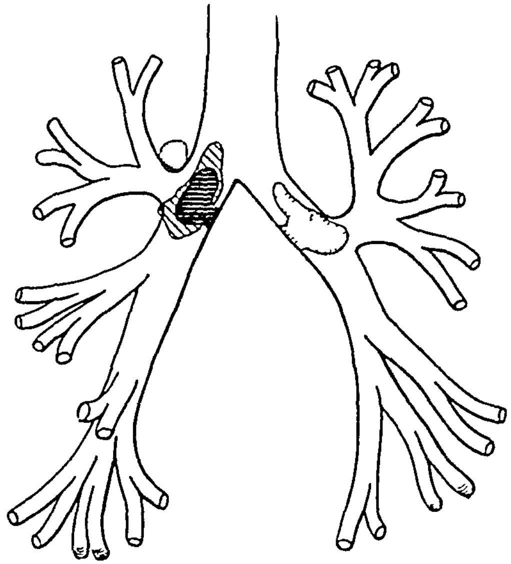


Fig 3.—*a*, Outline of tumor involvement in seven specimens of lungs from patients with adenoid cystic carcinoma *b*, Location and gross form of four muco-epidermoid tumors

and when it occurred, small bronchi appeared as cylinders filled with inspissated secretions passing through a dense mass of tumor. Occasionally peribronchial lymph nodes were included in the tumor and showed gross involvement. In one of the seven specimens, tumor was evident on gross inspection in a large pulmonary vein. It was apparent from the operative

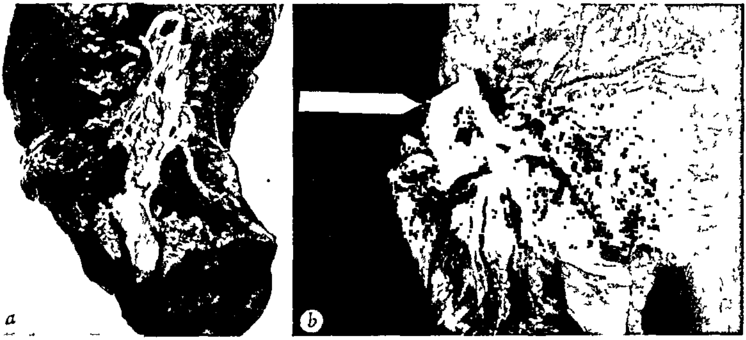


Fig. 4.—Specimens of lung from 2 patients with adenoid cystic carcinoma. a, Nodular and polypoid infiltrative tumor in right lower lobe bronchus (Case 7). *b,* Peribronchial thickening and carinal involvement by tumor (Case 12).

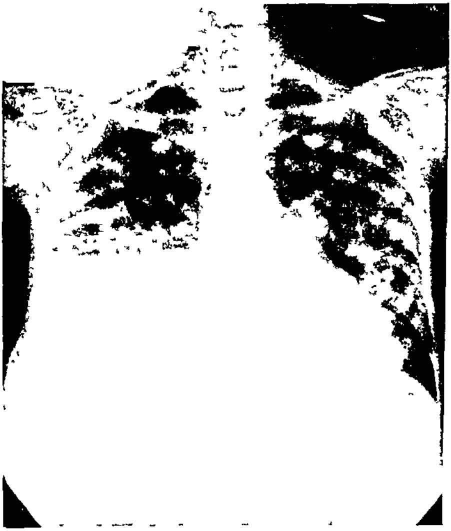


Fig 5.—Extensive involvement of remaining lung 6 years after right middle and lower lobectomies for adenoid cystic carcinoma (cylindroma) (Case 11)

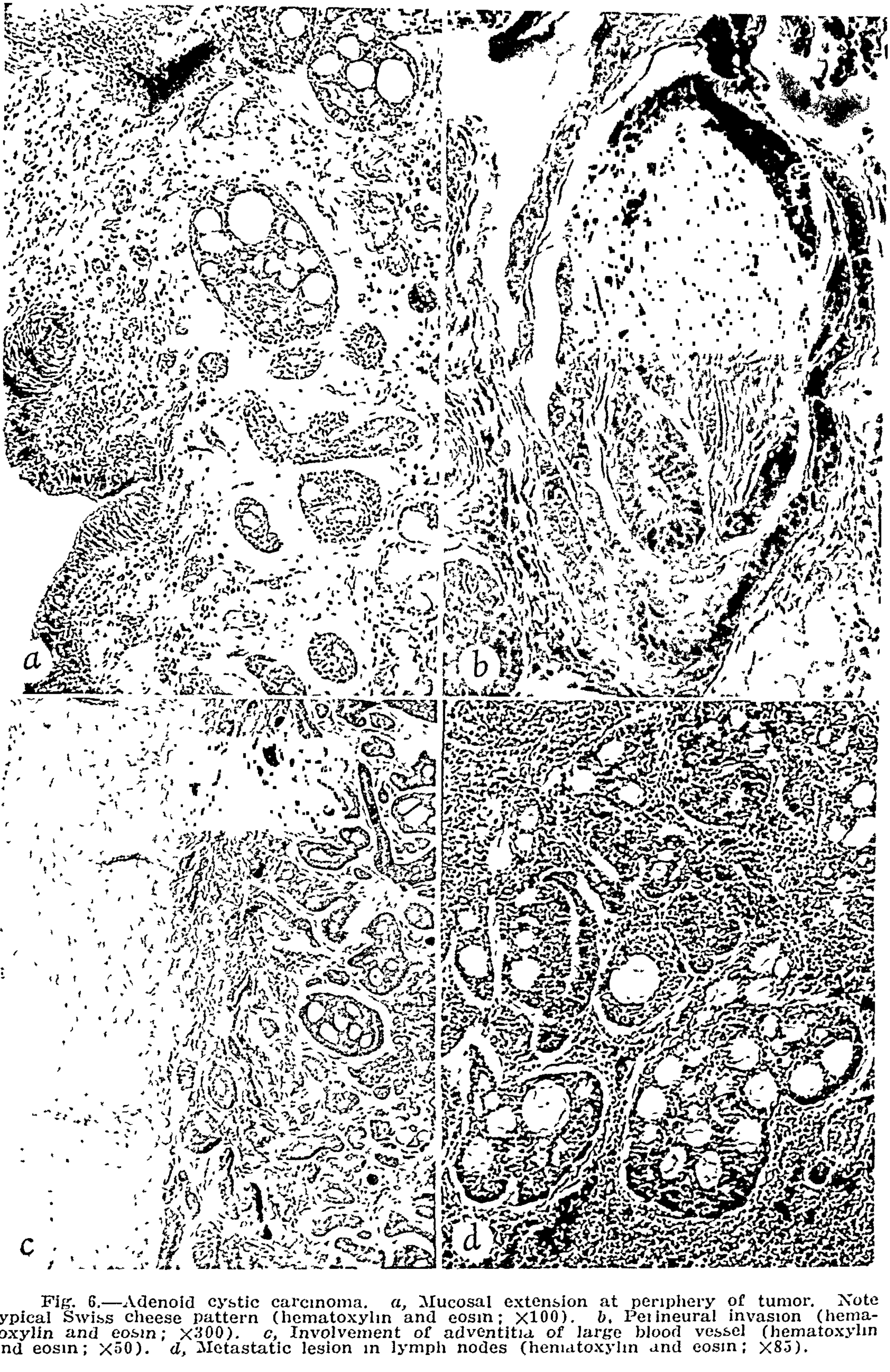


Fig. 6.—Adenoid cystic carcinoma. *a*, Mucosal extension at periphery of tumor. Note typical Swiss cheese pattern (hematoxylin and eosin; ×100). *b*, Perineural invasion (hematoxylin and eosin; ×300). *c*, Involvement of adventitia of large blood vessel (hematoxylin and eosin; ×50). *d*, Metastatic lesion in lymph nodes (hematoxylin and eosin; ×85).

reports or data obtained at the time of necropsy that four of the seven tumors showed gross involvement of mediastinal nodes, pericardium, or esophagus.

In addition to the six gross specimens of lung, material was available from necropsy on 2 patients treated by surgical resection. One (Case 7) who had died 10 months after pneumonectomy showed no evidence of residual tumor. The other (Case 11) had died 8 years after right middle and lower lobectomies, performed elsewhere. At the time of examination at the Mayo Clinic, extensive bilateral thoracic and hepatic involvement was apparent (Fig. 5) with jaundice and ascites. At necropsy, in addition to the thoracic involvement, extensive metastasis to the liver and peritoneum was found.

Microscopically, all of these lesions had the typical histologic features of adenoid cystic carcinoma. At the margins of the gross tumor there was extensive subepithelial infiltration of the mucosa (Fig. 6, *a*). In addition they all showed deep penetration and peribronchial extension with destruction of bronchial cartilages and invasion of neural elements (Fig. 6, *b*). Although tumor invasion of a vein was noted grossly in one specimen, none of the other six showed microscopic evidence of intravascular penetration, although all showed involvement of the adventitia and media of large blood vessels (Fig. 6, c). Peribronchial lymph nodes were involved by direct extension in four of the seven specimens and, in a fifth, embolic bronchial lymphatic metastasis had occurred (Fig 6, *d*).

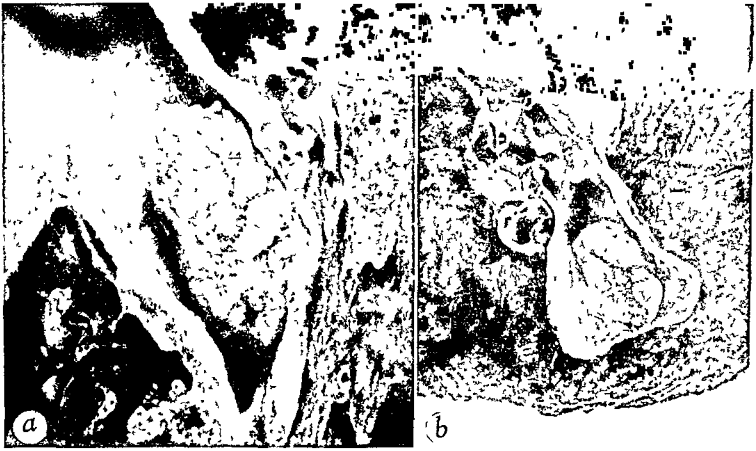


Fig 7.—Two muco-epidermoid tumors *a*, Postmortem specimen, right main bronchus viewed posteriorly (Case 14). *b*, Surgical specimen removed at pneumonectomy (Case 16)

Five of the seven specimens of lung did not show gross involvement of the tracheobronchial junction, but on microscopic examination, tracheal extension was apparent in three. Thus, of the seven specimens of lung only two were free of tracheal extension.

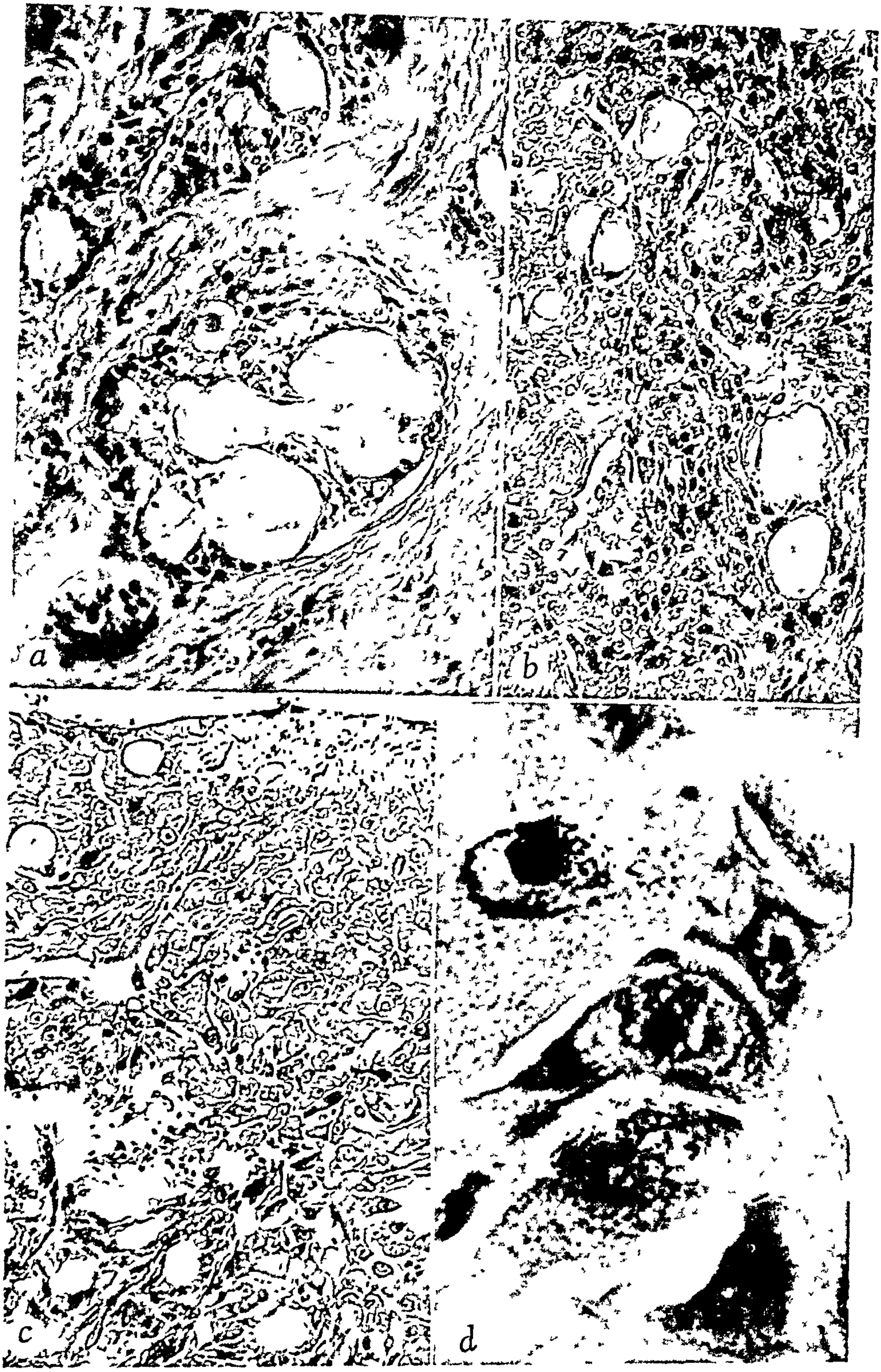


Fig. 8.—Muco-epidermoid tumor (hematoxylin and eosin). *a*, Two lines of differentiation should be noted (×300). *b*, Selected area with slightly less production of mucus (×300). *c*, Another tumor showing mainly squamous differentiation (×100). *d*, Same lesion as *c* showing intercellular bridges in squamous portion (×1,700). (This illustration has been reduced ⅒.)

Of further interest was the finding that the metastatic lesions of adenoid *cystic carcinoma retain the typical histologic features of the primary tumor.*

Muco-epidermoid Tumors.—In 2 of the 4 patients with muco-epidermoid tumors of the bronchus, surgical reports and surgically removed gross specimens of lung were available and data concerning the other 2 were obtained at the time of necropsy.

The distribution and gross form of these four tumors is illustrated in Fig. 3, *b*. The muco-epidermoid tumor in each of 3 cases appeared on gross inspection as a pedunculated polypoid endobronchial mass that completely occluded the bronchial lumen (Fig. 7). These tumors were covered with intact bronchial epithelium. As said before, the fourth muco-epidermoid tumor was situated extrabronchially and produced bronchial obstruction by extrinsic compression of the bronchus. None of the four muco-epidermoid tumors showed gross evidence of nodal extension or distant metastatic invasion.

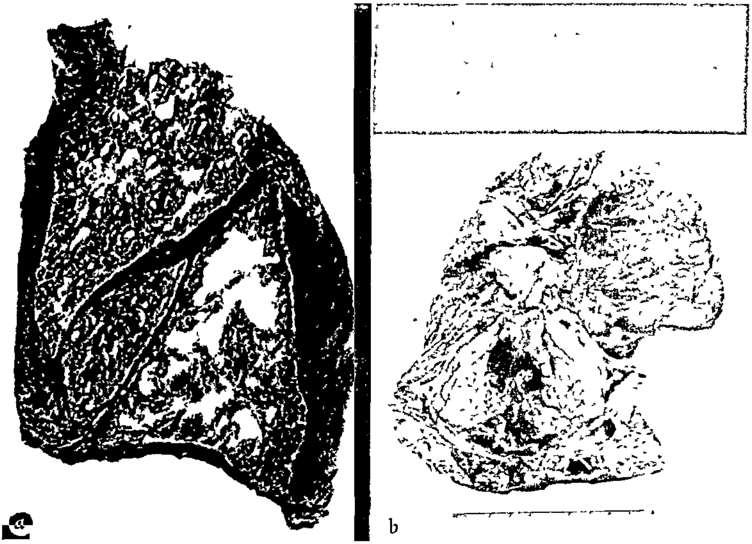


Fig 9 —Suppurative pulmonary complications. *a*, Lung of patient with muco-epidermoid tumor showing extensive bronchiectasis and multiple pulmonary abscesses (Case 14). *b*, Resected lung of patient with adenoid cystic carcinoma showing large abscess in left lower lobe (Case 6).

Microscopic section showed these tumors to be covered with metaplastic squamous bronchial epithelium (Fig. 8). Sections through the site of attachment of endobronchial tumors to the bronchial wall showed extension of the tumor outward between, but not beyond, the bronchial cartilages with minimal infiltration at the edges in two of the three. The third endobronchial tumor extended to the bronchial cartilages, but not between or beyond. The extrabronchial muco-epidermoid tumor on microscopic examination was intimately associated with deep bronchial glands. It did not encroach on cartilages nor did it have signs of infiltration about its margins. None of the four muco-epidermoid tumors showed destruction of cartilage or involvement of nerves, lymph nodes, blood vessels, trachea, mediastinal structures, or distant organs.

Pathologic Evidence for Pulmonary Suppuration.—The lungs of patients with adenoid cystic carcinoma and muco-epidermoid tumors showed the sequelae of bronchial obstruction. Bronchiectasis and obstructive pneumonitis were present in all specimens. In addition, four of the seven lungs of patients with adenoid cystic carcinoma and all four of those with muco-epidermoid tumors showed multiple abscess formation and extensive destruction of pulmonary tissue (Fig. 9). In one specimen pulmonary suppuration had progressed to the formation of bronchopleural fistula and chronic empyema (Case 15).

TREATMENT AND PROGNOSIS

In studying the prognosis in cases of adenoid cystic carcinoma and muco-epidermoid tumors of the bronchus, each group was divided into two subgroups, those in which treatment was surgical (pneumonectomy or lobectomy) and those in which treatment was more conservative (endoscopic surgical diathermy, radium, or roentgen ray).

Follow-up data in the form of one of the following was available during 1958 on all of the patients in this study: (1) recent examination at the Mayo Clinic, (2) reply to follow-up letters with accompanying recent thoracic roentgenogram, or (3) report of death. No patient was lost to follow-up.

Of the 13 patients who had primary adenoid cystic carcinoma, 7 underwent pulmonary resection. Six had pneumonectomy and 1 had right middle and lower lobectomies (Table V). The other 6 were treated conservatively because of the extent of their disease. The extent of the lesion of 1 patient did not permit resection at the time of surgical exploration; 4 had tracheal extension at the time of bronchoscopy and 1 had metastasis to the central nervous system at the time of diagnosis.

TABLE V. RESULTS OF TREATMENT OF CYLINDROMA (ADENOID CYSTIC CARCINOMA) AND MUCO-EPIDERMOID TUMORS

TUMOR AND TREATMENT	TOTAL PATIENTS	RESULT		AVERAGE SURVIVAL (YEARS)
		ALIVE	DEAD	
Adenoid cystic carcinoma				
Resection	7	4	3	4.8
Conservative	6	0	6	2.8
Muco-epidermoid tumors				
Resection	2	2	0	9.0
Conservative	2	0	2	2.0

The survival of patients with adenoid cystic carcinoma following various forms of treatment is summarized in Table V. At the time of the follow-up study 4 of the 7 patients surgically treated were alive and well 1 to 13 years after treatment. The average duration of survival for this group was 5.2 years.

Three of the 7 patients treated by surgical resection were dead within 1 to 8 years. The average duration of survival for the 3 dead patients was 4.3 years following treatment.

None of the 6 patients treated conservatively for adenoid cystic carcinoma of the bronchus was alive at the time of follow-up. The duration of survival of these patients ranged from 1 week to 11 years following initial treatment.

The average duration of survival for all patients, both those living at time of follow-up and those dead, who had been treated by resection for adenoid cystic carcinoma of the bronchus, was 4.8 years. The average survival for all of those receiving conservative treatment was 2.8 years.

Two of the 4 patients with muco-epidermoid tumors of the bronchus were treated surgically, and 2 conservatively (Table V). Both patients treated surgically had pneumonectomies and both were living and well 8 and 10 years following treatment. Neither of the 2 patients treated conservatively was alive at the time of follow-up. One died 2 weeks after diagnosis and initial treatment; the other survived 4 years. Both of these patients had technically inoperable conditions, 1 because of acute sepsis and respiratory insufficiency and the other because of previous bronchopleural fistula, empyema, and thoracoplasty.

Certain considerations which influenced ultimate prognosis and reflected the nature of the tumors are worthy of comment. Sepsis and respiratory insufficiency secondary to bronchial obstruction and pulmonary suppuration were the major causes of death of patients treated by conservative means, irrespective of the type of tumor.

The other consideration influencing ultimate prognosis was the relative malignancy of the two types of tumor. In 3 of the 13 patients with adenoid cystic carcinoma, widespread metastasis developed. In only 2 of the 7 patients surgically treated was it possible to remove all the tumor. Only 1 of the 4 surviving patients with adenoid cystic carcinoma was believed to be free of tumor (Case 6). The remaining 3 had residual tumor, but all were in apparent excellent health at the time of follow-up, 1, 2½, and 4½ years after resection, and the thoracic roentgenograms showed no evidence of disease.

There was no evidence of distant spread in any of the patients with muco-epidermoid tumors. Although 2 showed rather minimal local invasion of the bronchus, none showed more distant extension. The 2 surviving patients were believed to have been cured of their tumor. The cause of death in the 2 patients treated conservatively was pulmonary suppuration. No evidence of metastasis was present at necropsy.

COMMENT

Adenoid cystic carcinoma behaves as a slowly growing, infiltrating malignant lesion; it invades adjacent structures in continuity, erodes cartilaginous tissue and penetrates nerve structures and, occasionally, blood vessels. Having a prolonged and insidious course, the adenoid cystic carcinoma ultimately metastasizes distantly. Contrary to the findings in the more malignant bronchogenic carcinomas,[19] vascular invasion was not a significant feature

Reid,[20] and Enterline and Schoenberg,[21] in an excellent review of adenoid cystic carcinoma of the bronchi and trachea, have confirmed the malignant nature of these tumors and have noted that they develop with equal frequency in both sites.

Clark, Clagett, and McDonald[22] reviewed 15 cases of primary tracheal cylindroma encountered at the Mayo Clinic. The cylindroma was found to be the second most common primary malignant lesion in the trachea and was characterized by slow growth and a prolonged course before the development of metastasis. Unfortunately, the results of both their study and the present one dealing with the bronchus show the inadequacies of present methods of dealing with primary tracheal tumors and the tracheal extension of bronchial tumors of this type. Of the 15 patients in their series who had tracheal cylindromas, 10 were dead at the time of the follow-up study. The majority of deaths were in patients treated by conservative means. Four patients were in good health at the time of follow-up, and all had had surgical excisions of their tracheal tumors.[22] Contrary to the conclusions of Vieta and Maier,[23] the results of these studies have not shown irradiation to be curative in any of these patients and have indicated that it is of questionable value in palliation.

Enterline and Schoenberg[21] made a selected collective review of 30 documented cases of cylindroma of the bronchus appearing in the literature. Nineteen patients were treated surgically. Sixty-three per cent were living free of disease, 21 per cent were living with tumor, and 15 per cent had died of their tumor at the time of the follow-up study. Of the 11 patients treated conservatively, 27 per cent were living and well, 27 per cent were living with tumor, and 45 per cent dead of tumor. Unfortunately, follow-up data in such studies are of limited value, but the figures do reflect the relative merit of pulmonary resection in palliation. It is inconceivable in the light of the present study to consider conservative therapy in any way curative.

Despite the poor ultimate prognosis of adenoid cystic carcinoma of the bronchus, pulmonary resection offers the best hope for cure and certainly the best chance for palliation. The bronchial obstructive sequelae seen in this series resembled that described by McBurney and associates[2] for carcinoid tumors. These complications alone were adequate reason for resection even if involved tissue was knowingly left behind. The evidence of suppurative disease was particularly impressive in the group treated conservatively. All but 2 of these patients succumbed to the suppurative complications of the disease before any evidence of metastasis became apparent. Although a number of patients gained intermittent relief of their bronchial obstruction over a period of years, none was improved beyond a state of pulmonary invalidism by conservative treatment. On the other hand, those patients whose lesions could be resected experienced immediate improvement. All of those surviving in spite of residual tumor are living active, useful lives.

We are aware of only 3 previous cases of muco-epidermoid tumors of the bronchus.[5, 24] The available data suggest that these neoplasms are of relatively low-grade malignancy, and none has spread beyond the bronchus. In the present study these tumors produced disability by bronchial obstruction and secondary pulmonary suppuration. The two tumors amenable to surgical treatment were completely removed, and the problem of tracheal extension was not present. If the patient's condition permitted, surgical resection of the lung was performed. Local excision of the tumor was not indicated in any of our cases because of the presence of marked pulmonary suppuration distal to the tumor.

SUMMARY

In the 32 years, 1927 through 1958, 162 malignant tumors originating in the bronchial mucous glands were encountered at the Mayo Clinic. One hundred forty-five of these were carcinoid tumors, thirteen were cylindromas (adenoid cystic carcinoma), and four were muco-epidermoid tumors of the bronchus. The present study is concerned primarily with the adenoid cystic carcinomas and the muco-epidermoid tumors.

The presenting symptoms of all patients were predominantly related to bronchial obstruction and pneumonitis, and roentgenographic studies demonstrated some pulmonary collapse in most patients of both groups. Bronchoscopically, the adenoid cystic carcinoma appeared as an infiltrative malignant lesion, whereas the muco-epidermoid tumor predominantly appeared as a pedunculated polypoid mass. All involved major bronchi.

Pathologic data concerning the adenoid cystic carcinomas confirmed the bronchoscopic appearance as that of an infiltrative malignant lesion. These tumors were extensively invasive of peribronchial structures and often showed tracheal extension and mediastinal involvement. That these tumors are capable of widespread metastasis was demonstrated in a number of patients.

Similarly the pathologic data on the muco-epidermoid tumors paralleled their bronchoscopic appearance. Three were pedunculated polypoid endobronchial tumors and one produced bronchial obstruction by external compression. Two of the tumors showed some signs of local invasiveness, but none showed metastasis or extension beyond the point of bronchial attachment. Bronchial obstruction distal to the tumor frequently led to severe inflammatory sequelae regardless of the nature of the primary tumor. Often these suppurative complications were extreme.

Pneumonectomy was the only form of treatment that was presumably curative in patients with either type of tumor. In contrast to patients with muco-epidermoid tumors, only a few patients with adenoid cystic carcinoma had lesions that were potentially curable. Excellent palliation was possible when surgical resection was done in spite of the persistence of residual tumor. All patients in both groups who were treated by conservative means (endoscopic surgical diathermy, radium, or roentgen therapy) died. Most of them died of the suppurative complications of their disease.

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(For Discussion, see page 739.)

BRONCHOGENIC CARCINOMA

An Aggressive Surgical Attitude

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INTRODUCTION

THE SURGEON who recommends a thoracotomy for bronchogenic carcinoma implies that the disease can be cured by resection. However, the recent medical literature reports that in about 40 per cent of operated cases resection could not or should not be performed. This discrepancy between intent and accomplishment—tragic to the patient—presents a challenge to surgical skill and judgment. Consequently, in the last 10 years we have gradually extended our technical efforts to perform resection in more and more far advanced cases.

The justification for this surgical attitude was based not only upon modern technical advances but, also, upon the favorable biologic behavior of the lesion which permitted extensive growth locally, yet without detectable systemic dissemination. Somewhat to our surprise, the morbidity and mortality rates remained acceptably low and, as a result of our determined effort to increase the resectability rate, a few additional patients appear to be cured and many lives prolonged.

DEFINITIONS, CLASSIFICATION, AND DESCRIPTION OF OPERATIONS

The surgical aspects of the literature on bronchogenic carcinoma are often difficult to evaluate because of ambiguous terminology. Various authors have used such terms as "operable," "resectable," "radical resection," "palliative," "curative," etc., in different contexts.

The term "resection," by definition, means the removal of a considerable portion of an organ, in contrast to removal of an entire organ. However, this term is in popular usage in both contexts, and in this report it is used to denote removal of a portion of a lung, an entire lung, and any other structures included in the surgical specimen.

Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

We recommend the use of the following terms in defining operative categories.

1. Standard resection.
2. Extended resection.
3. Noncurative resection.
4. Palliative resection.
5. Explored only.

These operations are defined in more detail below.

1. *The "Standard Resection."*—Patients in this category were considered at operation to be *potentially cured* and the surgical specimen consisted only of pulmonary structures, parietal pleura when adherent, and mediastinal lymphatic tissue. Bronchoplastic procedures and resections of the tracheal carina were the only exceptions to these criteria and were not included in this category.

Mediastinal lymph node dissection was usually performed in the standard resection but not of the en bloc type. We arbitrarily divided this maneuver into upper and lower mediastinal dissections. The lower dissection was most often performed, and consisted of the removal of the lymph nodes inferior to the azygos vein on the right side and to the aortic arch on the left. It included periaortic, periesophageal, subcarinal, distal retrotracheal, and peribronchial nodes from the opposite main-stem bronchus. The upper dissection was of the mediastinal lymph nodes along the trachea and superior vena cava; these were removed whenever there was suspicion that they were involved and whenever the primary tumor was adjacent.

2. *The "Extended Resection."*—Patients in this category were also considered at operation to be *potentially cured.* Complete resection in these cases required removal of extrapleural structures invaded by carcinoma. The surgical specimens therefore included various combinations of pulmonary structures, portions of trachea, pericardium, atrium, intrapericardial vessels, chest wall, diaphragm, and esophagus. A mediastinal lymph node dissection, as described above under "standard resection," was done routinely when the "extended" procedure was carried into the mediastinum. Bronchoplastic procedures and partial resections of the trachea were included in this category.

3. *The "Noncurative Resection."*—Patients in this category were considered to be *potentially curable preoperatively,* had resection, but at operation were found to have additional inaccessible carcinoma. Frequently, this observation could be made only after removal of the major specimen. However, sometimes the observation of surgical incurability could be made immediately upon opening the hemithorax, yet removal of the major lesion was considered justifiable to avert secondary complications such as obstructive pneumonitis, abscess, obstructive emphysema, pain, and hemorrhage. Furthermore, it was considered advantageous to remove the major lesion so that radiation therapy could be confined to the mediastinal contents and thus avoid radiation complications in the residual lung.

The "noncurative resection" group was subdivided into the "standard" and "extended" procedures for the purpose of compiling operative complications and mortality rates. However, it seemed illogical to subdivide this group for the assessment of survival statistics, since none of the patients was considered to be potentially cured at operation.

4. *The "Palliative Resection."*—Patients in this category were known to be *incurable prior to thoracotomy* because of remote metastases, pleural effusion containing malignant cells, contralateral pulmonary metastases, or other unequivocal criteria of incurability. Resections were performed in this group *not* to treat bronchogenic carcinoma per se, but to palliate symptoms such as intractable cough, pain, hemorrhage, and uncontrollable infection that were secondary to the presence of the carcinoma.

We reasoned that the "noncurative" resections should not be included in the "palliative" category, since many of these patients did not have symptoms requiring immediate palliation, and, furthermore, they were considered to be potentially curable preoperatively in contrast to the palliative group as defined.

5. *The "Explored Only" Category.*—Patients included in this category were also considered to be *potentially curable preoperatively*. However, resection was not done in this group either because the findings were such that an early fatal outcome could be predicted before secondary local complications developed, or because the widespread dissemination of carcinoma precluded effective radiation therapy (diffuse pleural implants).

This report concerns 248 thoracotomies that are grouped according to the above operative categories. The operations performed and their relative frequencies are recorded in Table I.

TABLE I. OPERATIVE CATEGORIES (248 CASES)

TYPE OPERATION	NUMBER	PER CENT	PER CENT RESECTED	PER CENT POTENTIALLY CURATIVE
Standard resection	120	48.4	77	61.7
Extended resection	33	13.3		
Noncurative resection	32	12.9		
Palliative resection	6	2.4		
Explored only	57	23.0		
Totals	248	100.0		

CASE MATERIAL

The 248 cases of bronchogenic carcinoma included in this report were private patients of the senior author (J. M. C.) and in each instance he was the operating surgeon. All patients who had a thoracotomy for this disease during the years 1949-1958 are included, except for 3 or 4 cases in which there was no tissue diagnosis. During this 9 year period approximately twice this number of thoracotomies for bronchogenic carcinoma was performed, either by the senior author in a consulting capacity or by resident or attending surgeons whom he assisted. These cases were excluded to avoid unpredictable variables related to technique.

The positive tissue diagnosis in each case was obtained by bronchoscopic biopsy, thoracotomy biopsy, or by resection of the lesion. The histologic diagnosis was based upon the most predominant cell type. The types and their relative frequencies were epidermoid carcinoma (54 per cent), adenocarcinoma (16 per cent), anaplastic carcinoma (24 per cent), and bronchiolar carcinoma (6 per cent). The latter group was included in this report since the bronchiolar origin is generally accepted by pathologists and since the criteria for operation were the same as those in the other histologic categories.

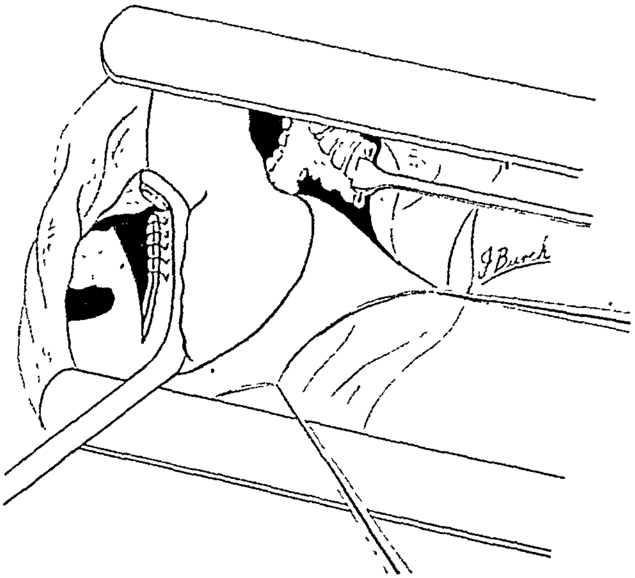

Fig. 1.—Resection of the left auricle in continuity with the right pulmonary veins. Carcinoma is shown invading the superior vein.

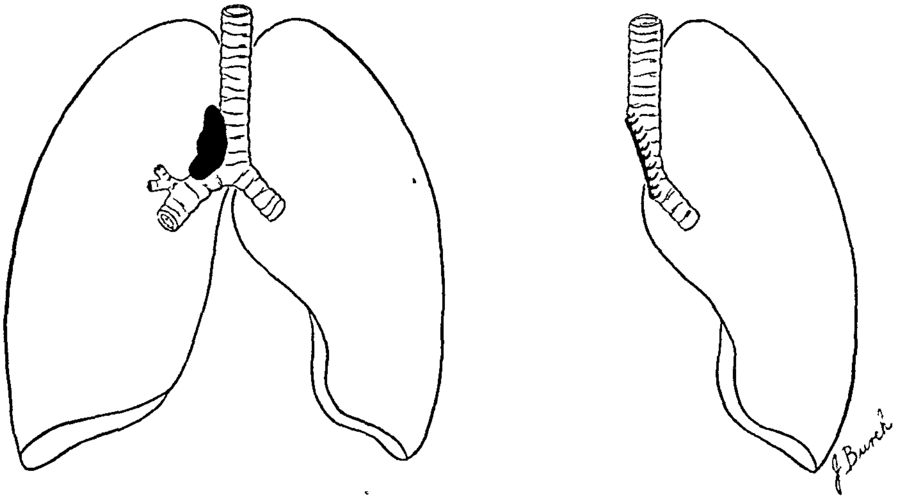

Fig. 2.—Resection of the tracheal carina and the lateral tracheal wall, with primary closure.

The sex incidence of bronchogenic carcinoma in this series was 222 in the male and 26 in the female, a ratio of 8.5:1. There was a relative preponderance of adenocarcinoma and bronchiolar carcinoma in the female. The mean age for males in this series was 57 and for females 51 years.

THE EXTENDED OPERATION

To encompass both the visible and palpable limits of the lesion it was necessary in some cases to perform an extended operative procedure by resecting the pericardium, atrial wall (Fig. 1) and, occasionally, if necessary,

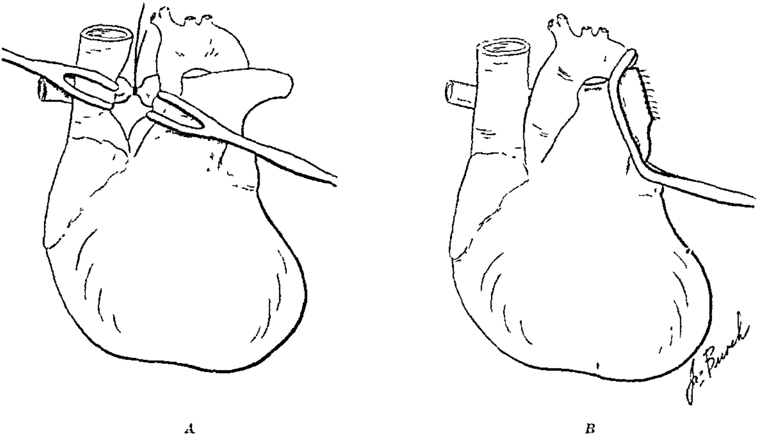

FIG 3.—A. The superior vena cava and the ascending aorta are retracted to permit proximal ligation of the right main pulmonary artery B, Partial occlusion of the pulmonary trunk to permit amputation of the left main pulmonary artery at its origin.

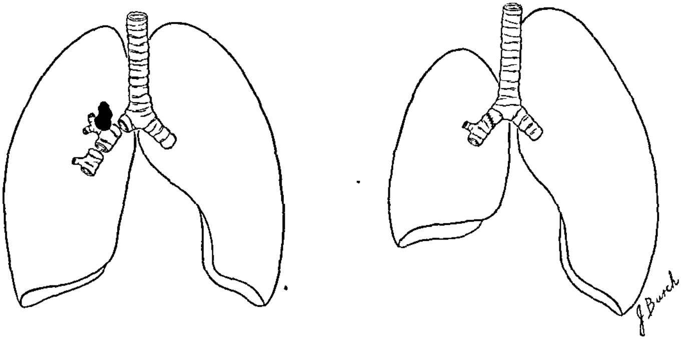

FIG 4.—Sleeve resection of the main bronchus in continuity with upper lobectomy. Anastomosis of the main and intermediate bronchi is shown preserving essential pulmonary function

the tracheal carina (Fig. 2) If the pulmonary artery was involved it was necessary to divide it at its origin (Fig. 3). In a few instances when the respiratory reserve was critically low, a sleeve resection of the main bronchus was included with the upper lobe. The intermediate bronchus then was anastomosed to the stump of the main bronchus in order to preserve pulmonary function (Fig. 4). On occasion we have found it necessary to include with the specimen a portion of the chest wall or the superior vena cava, and others who have reported on this subject have resected a portion of the diaphragm, a branch of the brachial plexus, short segments of the superior vena cava, the pulmonary artery, and even the aorta. We believe that all such maneuvers should be included in the armamentarium of the modern thoracic surgeon.

As a rule, we did not recommend thoracotomy for patients who had distant metastases, superior vena caval obstruction, involvement of the brachial plexus, left recurrent nerve paralysis, obvious cardiac failure, respiratory insufficiency, and uncontrollable extrathoracic systemic disease, such as nephritis and cirrhosis. However, the presence of bloody pleural effusion without malignant cells, paralysis of the phrenic nerve, or history of a proved coronary occlusion was not, in our opinion, an absolute contraindication to an exploratory thoracotomy. Such cases required individualization.

OPERATIVE MORBIDITY

The complete morbidity of a surgical procedure is sometimes difficult to assess, for it depends not only on the effect of trauma inflicted on the body but also on a subjective response, in the mind of the patient. The latter factor is intangible, but is common to every operation. We believe, therefore, that the mean duration of hospital stay and the incidence of major complications give as reliable an indication as can reasonably be obtained of any trend in morbidity that the "extended" operation might produce. Table II shows that the mean duration of postoperative hospital stay was not increased significantly by extending the operation.

TABLE II. BRONCHOGENIC CARCINOMA
POSTOPERATIVE DAYS IN HOSPITAL

Explored only	12.5
"Standard" resection	14.4
"Extended" resection	15.4
Palliative resection	14.2

Major operative complications encountered in this series of 248 cases, including the 23 which were fatal, are arranged in Table III according to the type of operation. There were five bronchopleural fistulas, three following right pneumonectomy and two following left upper lobectomy. Two of these responded to conservative management and two required thoracoplasty. The fifth was fatal. Nonfatal empyema without demonstrable bronchial fistula occurred twice, and in only 1 case was thoracoplasty required. Two additional cases were fatal. One wound infection occurred in the entire series (0.4 per cent). Postoperative hemorrhage that required re-exploration for its control occurred three times. Fatal hemorrhage at operation occurred once. Only 2 patients had a postoperative myocardial infarction, 1 is still living 2½ years after an "extended" pneumonectomy that included pericardium involved by carcinoma, and the other patient died. The additional complications that occurred in this series were fatal. These are described in the section on operative mortality.

TABLE III. OPERATIVE COMPLICATIONS

COMPLICATION	TYPE OF OPERATION* STANDARD (142)	EXTENDED (43)	EXPLORED (57)	TOTAL (248)
Cardiac arrest	1	0	0	1
Herniation of the heart	0	1	0	1
Hemorrhage	2	2	0	4
Bronchopleural fistula	5	0	0	5
Empyema	2	2	0	4
Wound infection	0	1	0	1
[illegible] pneumonia	1	1	0	2
Respiratory failure	5	1	2	8
Pulmonary embolus	1	2	0	3
Myocardial infarction	1	1	0	2
M[illegible]	1	2	0	3
T[illegible]	19	13	2	34
P[illegible]	13.4	30.2	3.5	13.7

*[illegible] complication in palliative group (6 cases).

The [illegible] relative frequency of complications in the "standard" and "extended" operations is also demonstrated in Table III. The numbers of each complication were too small to exclude fortuitous occurrences, however, no alarming incidence was noted in the "extended" group. The complication rate for the "extended" operations was 30.2 per cent compared with 13.4 per cent for the "standard" operations. No complication occurred among the 6 cases of "palliative resection." Two fatal complications occurred among the 57 explored cases (3.5 per cent). The over-all complication rate for the 248 cases in this report therefore was 13.7 per cent.

OPERATIVE MORTALITY

Operative death in this report is defined as death occurring from any cause during operation or while still in the hospital postoperatively.

Hospital deaths numbered 23 among the 248 operations, a total mortality rate of 9.3 per cent. Table IV lists the causes of death and the respective mortality rates according to the type of operation. Three deaths occurred [illegible] operation, one due to herniation of the heart after partial pericardiec[illegible] [illegible] due to exsanguination that occurred when lung retraction avulsed [illegible] comprised the right atrial wall, and the third was due to cardiac [illegible]

Bronchopleural fistula complicated by pneumonia caused death in 1 case [illegible] "standard" left upper lobectomy. Two patients died after a [illegible] with empyema, complicated by septicemia in 1 case and [illegible] other by [illegible]olitis.

[illegible] deaths [illegible] attributed to cardiac or respiratory insufficiency. Only [illegible] of these patients had an "extended" operation. Bronchopneumonia following pneumonectomy was fatal to 2 patients, 1 in each of the resected categories. Three patients died from pulmonary embolus, 2 of whom had "extended" surgery. Fatal myocardial infarction, 5 days after a "standard" pneumonectomy, occurred once.

TABLE IV. OPERATIVE MORTALITY

CAUSES OF DEATH	TYPE OF OPERATION* STANDARD (142)	EXTENDED (43)	EXPLORED (57)	TOTAL (248)
Herniation of the heart	0	1	0	1
Cardiac arrest	1	0	0	1
Exsanguination	0	1	0	1
Bronchopleural fistula	1	0	0	1
Empyema	2	0	0	2
Cardiorespiratory failure	5	1	2	8
Bronchopneumonia	1	1	0	2
Pulmonary embolus	1	2	0	3
Metastases	1	2	0	3
Myocardial infarction	1	0	0	1
Totals	13	8	2	23
Per cent	9.1	18.6	3.5	9.3

*No mortality in palliative group (6 cases).

Distant metastases became evident postoperatively in 3 cases. In 1 of these, the bowel ruptured at the site of serosal implantation and death was caused by peritonitis. Carcinomatosis was fatal 1 month postoperatively for 1 patient and metastases became evident in the brain of another and caused death after 6 weeks.

The relative occurrence of hospital deaths in the "standard," the "extended," and the "explored" categories is listed in Table IV. Thirteen deaths among the 142 "standard" resections represented a mortality rate of 9.1 per cent, whereas the 8 deaths among the 43 patients having "extended" resections represented a mortality rate of 18.6 per cent. These deaths, plus the 2 among the 57 explored cases (3.5 per cent), comprise a total mortality of 9.3 per cent for the 248 operations. No hospital deaths occurred among the 6 incurable patients whose operations were performed only for palliation of symptoms.

The first five causes of death listed in Table IV were considered to be directly attributable to the type of operation performed. Table V lists operative deaths due to surgical technique and other causes for each type of operation. This will be referred to in the final discussion.

TABLE V. OPERATIVE MORTALITY

OPERATION	SURGICAL TECHNIQUE (PER CENT)	OTHER CAUSES (PER CENT)	TOTAL (PER CENT)
Standard resection (142)	2.1	7.0	9.1
Extended resection (43)	4.6	14.0	18.6
Explored only (57)	0.0	3.5	3.5
Totals* (248)	2.0	7.3	9.3

*No mortality in palliative group (6 cases).

SURVIVAL

Just as the total operative morbidity of any surgical procedure is incompletely assessed from a statistical aspect alone, so are survival statistics following thoracotomy for bronchogenic carcinoma only a partial indication of its over-all merit. Those patients whose carcinomas were amenable to potentially curative resection and who survived without radiation therapy for at least 3 years with no recurrence, probably survived as a result of the operation. These cases are the ultimate reward of a surgeon's efforts, and should make every thoracic surgeon operating on bronchogenic carcinoma determined to accomplish as many potentially curative resections as possible. In this report, 13.3 per cent of all our patients achieved a "potentially curative" status by means of an "extended resection" (Table I). The postoperative follow-up period of this series is too brief at present to permit even a 3 year appraisal of the majority of "extended resections." However, general trends of survival could be determined and are presented in Table VI.

TABLE VI. SURVIVAL

OPERATION	NUMBER LEAVING HOSPITAL*	NUMBER LIVING	NUMBER 3-8 YEAR SURVIVORS	MEAN SURVIVAL (MO.)
Standard resection	110	40	22	21.6
Extended resection	26	13	2	16.7
Noncurative resection	28	1	1†	11.5
Palliative resection	6	0	0	4.4
Explored only	55	3	2†	8.8

*Excludes operative deaths.
†Radiation therapy.

The patients who had a "standard resection" have a mean survival of 21.6 months to date, 36.7 per cent of these patients are still living and remain potentially cured. The patients who had an "extended resection" have a mean survival of 16.7 months to date, 50 per cent of these patients are still living and are potentially cured. There are 22 3 year survivors of the "standard resection" group and only 2, thus far, in the "extended resection" group. A major factor in the differences in these figures is the more recent introduction of the "extended resection."

The comparable survival statistics for patients not potentially cured at operation are impressively low in each category. Of 28 patients in the "noncurative" resection group, only 1 patient is living, and he is known to have diffuse contralateral lung metastases. Only 1 patient in this group survived longer than 3 years, and he succumbed to carcinomatosis after 4 years and 2 months. The mean survival following "noncurative resection" was 11.5 months. Most of these patients received radiation therapy postoperatively.

The patients who had exploratory operations without resection survived an average of 8.9 months. The 3 survivors in the "explored only" group are especially interesting since they have no counterpart in the "noncurative resection" group. These 3 patients are males who had right upper lobe infiltrating carcinomas. They received radiation therapy and remain clinically well without evidence of metastases or increasing local growth. They have survived 4 years, 3 years and 7 months, and 1 year, respectively.

DISCUSSION

The increasing incidence of bronchogenic carcinoma in this country fortunately has occurred during an era of rapid advances in thoracic surgical technique. The recent trend toward earlier diagnosis has increased the chances of successful surgery in many cases. However, the reported number of patients who were *not* potentially cured by surgery remains high. This report concerns especially the use of an "*extended resection*" for patients who would have been incurable by standard lung resection techniques.

Carcinoma in any organ may behave in unpredictable ways. When one considers that lung tissue is made up entirely of blood, lymphatic and air channels, it would seem especially remarkable that a lung carcinoma could ever grow large *without* clinical evidence of systemic dissemination. Yet this is often the case, and this phenomenon must indicate the relative benignity of these extensive local growths. Perhaps such cases deserve especially the application of every available thoracic surgical technique to effect a potentially curative resection.

We believe that there should be a *universally accepted nomenclature* that would portray the accomplishments of the surgeon, and which should not be determined or influenced by the delayed but final report of the pathologist. This qualification would seem practical since the surgeon decides the dimensions of the operation at the operating table without microscopic control to define the limits of the carcinoma. The terminology for operative categories submitted in this report permits clear-cut allocation of each case, and permits relative assessment of the maximum surgical efforts to cure bronchogenic carcinoma.

We did not consider it useful to include in the terminology reference to the amount of lung tissue removed, i.e., pneumonectomy, lobectomy, and segmental resection. These operative terms more often reflect the fortuitous position and nature of the primary lesion, rather than the surgeon's accomplishment in removing all carcinoma possible.

The terms "standard resection" and "extended resection," according to the definitions presented, include the only patients who were considered to be potentially curable at the time of operation. These cases alone, therefore, represent surgical accomplishment, and this might be best expressed in terms of a "*potentially curative resection rate.*" This was 61.7 per cent for this series of 248 cases. The total resectability rates (77.0 per cent in this report) that usually are recorded in the literature are meaningless from the standpoint of surgical accomplishment, since usually there is no indication of how many noncurative resections were included.

"Extended resection" techniques achieved, in this series, a potentially curative status for 26 patients. These patients would have been incurable by standard techniques of pulmonary resection. The operative complications and mortalities incurred to establish this group were approximately twice the rates for the "standard resection." The mortality rates consequent to the "standard" and the "extended resections" were 9.1 and 18.6 per cent, respectively (Table IV). However, even these rates were acceptably low, especially when the complications that were fatal and directly attributable to surgical technique were considered separate from those causes of death that might be expected following any major operation (Table V). Listed in this fashion, mortality rates were 2.1 per cent and 4.6 per cent, respectively, for the "standard" and the "extended resections."

Continued experience with bronchial and cardiovascular techniques should permit fewer complications among the "extended resections." We have learned, for example, to close large pericardial defects with parietal pleura to prevent herniation of the heart, and to use electrocoagulation almost routinely just prior to closing the thorax for more complete hemostasis in the extrapleural planes and on raw lung surfaces. Careful observance of the basic principles of bronchial closure was essential to maintain a low incidence of bronchopleural fistula.

A note of caution is indicated for the bronchoplastic procedures in which sleeve resection and bronchial anastomosis were performed to preserve lower lobe function. We consider that this procedure should be used only when the respiratory reserve is such that pneumonectomy could not possibly be tolerated.

Several years must pass before the customary 5-year survival data can be compiled for this series of cases. The trends that are apparent in Table VI constitute sufficient evidence, in our opinion, to state that the "extended resection" not only is justifiable but definitely is indicated whenever it is technically possible. The alternative for these patients is to abandon hope entirely and to deny them and their families the satisfaction that everything possible surgically was done.

SUMMARY

In the surgical treatment of bronchogenic carcinoma, it is not our intent to encourage unguarded aggressiveness in the modern thoracic surgeon. During the past 25 years the indications for and against thoracotomy have been fairly well standardized. The 248 cases in this report probably would have been selected for operation by the majority of experienced thoracic surgeons.

The biologic behavior of bronchogenic carcinoma is often paradoxical; it may become extensive and invasive locally without detectable systemic dissemination. In our opinion, such lesions deserve an extended surgical effort to accomplish complete removal.

Twenty-six patients in this series were afforded a potentially curative status by extended surgical efforts without unduly increasing the operative morbidity and mortality.

The favorable survival pattern in this group encourages us to recommend this aggressive surgical attitude.

Once a patient has accepted our surgical recommendation, we are obliged to justify his confidence by including in our surgical armamentarium the techniques outlined.

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DISCUSSION

(PAPERS BY PAYNE [PAGE 709] AND CHAMBERLAIN [PAGE 727] AND THEIR ASSOCIATES)

DR FREDERICK R HARPER, Denver, Colo —I would like to congratulate Dr Chamberlain for bringing this to our attention at this time, after Julian Johnson s very discouraging paper of 2 years ago

I am sure we all have performed extended resections after which the patients survived for some years The thing that disturbs me is that, for the past few weeks at the Louisville General Hospital, the Pathology Department has been making examinations of the peripheral blood for cancer cells by a technique that has been well described, and in bronchogenic carcinomas the incidence of cancer cells in the circulating peripheral blood is perfectly tremendous What the significance of these cells is we don t know We obviously know from this report and our own work that they do not all survive—that is, these cells—and I hope that more of you will get interested in your institutions and run these sections so that within a very short time we can get some idea of the value or the implications of these carcinoma cells in the peripheral blood.

DR. DONALD L. PAULSON, Dallas, Texas.—My purpose in discussing Dr. Chamberlain's excellent presentation is to emphasize the futility and the possible harm from an overly aggressive attitude in the surgical treatment of bronchogenic carcinoma, and to urge an approach based on, or at least tempered by, the biologic factors of cell type, location of the lesion, and the extent of the lesion.

Certainly one is justified, as emphasized by Dr. Chamberlain, to resect a low-grade epidermoid carcinoma by means of a radical resection in contrast to the small-cell undifferentiated carcinoma, which rapidly disseminates distantly.

This slide shows the operability rates in our series of 1,180 cases from 1946 through 1957, and our experience has revealed a resectability rate, up until 1951, of those patients operated upon of 64 per cent. In the years 1951 through 1955, this rose to 74 per cent for all operations for carcinoma. The operability rate remained close to 50 per cent.

The year 1954 is particularly interesting because we found our resectability rate rising to 83 per cent of all patients operated upon. We felt that this was indicative either of a more aggressive attitude on our part, or that we were dealing with more favorable lesions.

[Slide] A follow-up of these patients operated upon in 1954 revealed no better survival rates than the general average for all the years. Of the 30 patients having pneumonectomy performed in 1954, 3, or 10 per cent, are alive in the fifth year, and of the 34 patients having lobectomy 9, or 26 per cent, are alive. Combining all resections for the year 1954, when our resectability rate was 83 per cent, 12 patients of 64, or 19 per cent, are alive in 5 years, which is the identical figure for all resections done from 1945 to 1956.

[Slide] The figure for all resections is 19 per cent survival for 5 years, lobectomy 23 per cent, and pneumonectomy 15 per cent.

In conclusion, I would like to emphasize the points made by Dr. Chamberlain, that whereas the resectability rate should be maintained at a high level and unwise exploration of a nonresectable carcinoma avoided because of its mortality and lack of benefit to survival time, the tendency on the part of the surgeon to extend the scope of operation and perform palliative resection, knowingly leaving behind carcinoma, is likewise to be deplored. Under these circumstances, and I think Dr. Chamberlain's figures illustrated this, the mortality rate of resections of this type rises close to 20 per cent and survival is no better and, in some instances, not as good as for the inoperable cases.

DR. MICHAEL E. DE BAKEY, Houston, Texas.—I should like to inject one thought here with regard to the evaluation of statistics of this kind, and this concerns again the definition of resectability rates.

Resectability rate of patients operated upon, of course, is one thing. Resectability rate in terms of all cases of carcinoma encountered is still another, and this is important, because obviously unless one relates the patients operated upon to the total number of cases encountered, the resectability rate can vary considerably. It is essential, therefore, to define the resectability rate in these terms, since obviously one can either increase or reduce the resectability rate of all patients operated upon by simply changing the criteria for operation upon all patients encountered.

DR. ALFRED GOLDMAN, Beverly Hills, Calif.—I would like to confine my discussion to the first paper, that of Dr. Moersch and his group.

In studying our group of cases of bronchial adenoma, we have felt that there are well-differentiated factors which, as Dr. Moersch and his group have shown, tend to separate off the cylindromata from the carcinoid group. One of the things which we have studied is the relationship of treatment as one finds the indications in these two groups of tumors.

As they have occurred to us, we have not found a cylindroma that has lent itself to local excision by bronchotomy. On the other hand, we have found 7 patients in whom the carcinoid histology occurred in which local excision via bronchotomy was a perfectly adequate treatment, and the follow-up in 5 of these has now reached more than 5 years and in 3 of them is approaching 10 years without the evidence of any demonstrable metastasis.

On the other hand resection of the cylindromatous type with lobectomy has not always been curative, even wh[illegible] [illegible] [e]xpected cure. In 1 patient recently, 7 years after resection, widespread metastasis [illegible] liver and death from cachexia due to generalized metastasis has already occurred.

It seems that th[illegible] differentiation in the behavior of these tumors is the real thing on which we can base treat[illegible]

DR JOHN H GIBBON JR, Philadelphia, Pa—I have a great deal of sympathy with Dr Chamberlain [illegible] about the radical approach to carcinoma of the lung. I don't think my sympathy [illegible] quite as far with regard to palliative operations but I am n[illegible] quite sure wh[illegible] Dr Chamberlain means by this term.

I [illegible]nk resection of the [illegible] veins as they enter the atrium, actually removing a part of [illegible] atrial wall is always [illegible]d if you cannot encompass the tumor otherwise. We excise [illegible]mor when we think that we can remove all gross and visible tumor in the heart.

I [illegible]ne so far is to resect the terminal end of the trachea in a right pneumon[illegible]tomosed the left bronchus to the residual trachea. I am sure this is a [illegible]re. This man died from extension 6 months later, and I am not sure how [illegible] him. On the other hand, I do think that we should be quite radical in our [illegible]ack out merely because it is a large tumor.

[illegible]ur group of 5 year survivals 7 patients in whom there was extension into [illegible]r to structures outside the lung. Two of this group had anaplastic

[illegible] I might just show our experience with cancer of the lung over the last 12 [illegible] here. These patients were operated upon by myself or members of my [illegible] including surgical residents, so they don't represent quite the type of patient [illegible] Chamberlain referred to in his paper. [illegible]sed the cancer in 40 per cent of all the patients we saw and our 5 year survival [illegible] per cent of the patients who survived the operations. [illegible]ink that Dr Chamberlain's point is well taken, that this is a disease which is [illegible]ill and if we can give the patient more years to live by being radical, then I [illegible]ly in favor of it. I would like to say also that we invariably do a really extensive [illegible]l node dissection, which I think is an essential part of the operation.

[illegible] LAMBERT, New York, N Y—I should like to discuss the second paper. [illegible]nk [illegible]ne presentation, and to say a few words about advanced lung cancer [illegible]a of [illegible] lung that has invaded the chest wall is extremely important to excise [illegible] tr[illegible] us pain that these patients have when this extension is left in. [illegible] le is [illegible]r line patient in whom there was invasion of the chest wall which [illegible]at pneu[illegible]my. He died a year and a half later without being cured of his [illegible]s cour[illegible] characterized by the excruciating pain which all too frequently

[illegible]tients to [illegible]ll like to make is that in the patients who have necrosis or [illegible]d point [illegible] that all effort be made to remove the primary tumor, [illegible]m their [illegible] glands and obvious malignancies in the mediastinum [illegible] may lea[illegible] nature in which the lower lobe tumor invaded the left [illegible] represents a [illegible] but, because of the patient's general condition, the [illegible]art. This wa[illegible] enlarged and involved right up to the [illegible]ls were left a

[Slide] The next slide shows part of the auricle with the tumor invading it that has been removed. The patient surprised me by not having further extension of his disease until 4 years later, when he developed a node in his neck which was positive for squamous cell carcinoma. Now 6½ years afterward, the patient is about to die of his disease, but in the interim he has been free of his symptoms, which included about a pint of purulent sputum a day and hemorrhage, which had required two transfusions a day for the 2 weeks preceding his operation.

[Slide] The third point I should like to make is that patients who may have blood vessel invasion who later develop a metastasis should have the metastasis considered solitary until proved otherwise. This patient has been commented on before but I show this to you as a follow-up.

This was a 26-year-old girl with adenocarcinoma of the left upper lobe, with no symptoms from her disease, who had been picked up as a contact.

This slide shows the type of adenocarcinoma that she had. We felt we had completely removed it with a left upper lobectomy, taking out about eight mediastinal glands, all of which were negative, until [slide] we saw the malignant cells present in the pulmonary vein. Therefore, we were on the lookout for metastasis so that [slide] 14 months later, when she came in with a cough, and this obvious metastasis in the right upper lobe on the other side, we removed the right upper lobe on that side. The tumor [slide] proved to be the same type as the original tumor.

She then went 6 years and wanted to have a baby. Physiologically, I felt she could withstand pregnancy and advised her to go ahead, which she did. The obstetrician sent her back to me when 4 months pregnant with a lump in the right breast which I thought was probably another metastasis, but in taking it out it proved to be a primary carcinoma of the breast. Radical mastectomy was performed with removal of internal mammary nodes and axillary nodes, all of which were not involved.

It is now 7 years following the primary resection of the breast, 13 years following the primary resection of her carcinoma, and 12 years following the metastasis, and the patient shows no further evidence of malignancy or pulmonary dysfunction.

DR. JULIAN JOHNSON, Philadelphia, Pa.—I certainly appreciate Dr. Chamberlain's paper. I agree with him in principle in the aggressive attitude toward carcinoma of the lung.

Lest there be some misunderstanding regarding our paper last year, we certainly never intended that one should not be aggressive in the removal of a tumor. Our point was that the presence or absence of blood vessel invasion in the tumor is very important in the prognosis. In our practice, if we could remove a tumor grossly at the time of operation we have done so, and that is perhaps attested to by the fact that our 5-year survival rate is 26 per cent, with an over-all 5-year survival of 9 per cent.

The point which we made last year is that so far no one has demonstrated the superiority of a radical operation, such as has not been talked about here but which consists of a widespread mediastinal dissection with removal of the lung and mediastinum en bloc even for an early lesion. Let us not confuse the term. The term ''radical pneumonectomy'' as proposed by Philip Allison is the widespread dissection for a small lesion, whereas being aggressive in getting a big lesion out is something entirely different. We have felt that one does not need to be obligated to do a wide dissection of the mediastinum, lymph nodes, and contralateral bronchus, take out the pericardium, and divide the vessels to the lung inside the pericardial sac in small lesions, and we ourselves have been doing more and more lobectomies for the small lesion. We have our highest 5-year survival rate in that group.

But as far as taking the big tumors out, we are not relieved of our obligation there in any way by these data which we gave on 5-year survival. We don't know at the time of operation whether there is blood vessel invasion or not, and if we have a huge tumor without blood vessel invasion and do not take it out, we have done a disservice to that patient.

This was attested to by 1 such patient in our series. I found, to my surprise, after I had terminated the operation and sent him home to die, that 5 years later he was still alive.

We went back and reviewed his tumor and he did not have blood vessel invasion in his tumo
I reviewed our operative note and found that he had had invasion of the right atrium whic
was the reason we stopped. If we had been a little more aggressive perhaps we could have
got this out and the man could have been saved. Although he is obviously going to die of his
tumor, he is still alive almost 6 years later with no resection at all. He had had no x-ray
treatment, no nitrogen mustard, or specific therapy of any kind.

DR ROBERT J JENSIK, Chicago, Ill—I came to this meeting anticipating a good
port by Dr Chamberlain and he certainly didn't disappoint me and I am sure he didn't
ppoint the rest of us.

I would like to sympathize with his approach to this problem and give him very
rt that is possible, and mention a few of our figures along this line. We have had
the same philosophy and, in comparing 5 year periods of 1949 to 1953 and 1953 to
e find that we have increased the resectability rate in the first group of 61 per cent
per cent in the second group.
the second group there were 282 thoracotomies and resection was accomplished
tients

patients represent private practice material entirely and we do have the oppor
omparing clinic material. Notoriously, clinic material does not give the sam
patient, because in many of them the disease is so far advanced our resectabilit
low as 60 per cent in that group.

ted to ask Dr Chamberlain about the problem of hoarseness, whether he was
ntraindication to a thoracotomy. We have felt that even if the patient demonst
paralyzed cord he was still entitled to an operative chance and in about 25 patients
plished resection in 10 of these. We have not had a single 5 year survival in a
whom hoarseness was a problem, the longest survival being 3 years.

R P LAURENCE K GROVES, Cleveland, Ohio—I should like to point out another are
guarded aggressiveness may be indicated.
[Slide] This is not, certainly, a typical Pancoast's syndrome, so-called, but this
rt chief complaint was pain in the region of the right shoulder. He had a lobectomy
the region of the pleural apex, where there was frank tumor left behind, as in
ated with radon seed. The date isn't all on there; it is December, 195

I had a letter from him last week. He is fine. When he started coming back about
ars later we got interested in trying this on some other patients. None of them has
as well as he has, but it has been impressive to us that if there isn't frank brachial
involvement it is surprising that even the next day, after you have [illegible] the tumor
the apex and put radon seeds in there seems to be a peculiar relief of pain, grea
ion and much more comfort.

R. AARON HIMMELSTEIN, New York
r Dr Chamberlain has
in th

this side being 33 per cent of the total. These cases have interested us particularly because they also offer one the opportunity to study a lung which has been largely denervated, since the pulmonary artery is stripped of its neural sheath and the only structure which is relatively undivided or untouched is the inferior pulmonary vein.

The relationship of circulation to ventilation in these lungs also is of great interest.

DR. JEROME R. HEAD, Chicago, Ill.—I would like to say a few words about Dr. Payne's excellent paper. It seems to me it is important in that it shows definitely the malignancy of the cylindromas and the mucoepitheliomas, but also because, by implication, it implied the nonmalignancy of the carcinoid tumors or the simple adenomas.

I feel that simple adenoma is never an indication for lung resection unless the lung has already been so damaged by bronchial destruction that it is past redemption. I agree with Dr. Goldman that, in these cases, a bronchotomy is the procedure of choice if the lesion cannot be removed through the bronchoscope.

I would like to mention one unusual procedure which we used in a case of this kind in a woman with a right upper lobe atelectasis. On bronchoscopy we found a simple adenoma protruding from the right upper lobe bronchus. At that time we were using flammable anesthetics and could not use diathermy. We did a bronchotomy and found that both the upper lobe bronchus and part of the main bronchus were involved with the tumor. We closed off the main bronchus and packed the intermediary bronchus; we then took a uterine curet and curetted the upper lobe bronchus. Bleeding, as is usual in these cases, was profuse and was uncontrollable at the time of operation, so we packed the upper lobe bronchus with gauze and left it in place, but attached a long string to it, which we brought out through the mouth. We left the pack in place for 48 hours and then withdrew it through the mouth.

DR. PAYNE (Closing).—I wish to thank Dr. Goldman and Dr. Head for their comments. Although we consider carcinoid bronchial adenomas, muco-epidermoid tumors, and cylindromas of the bronchus to be distinct and separate clinical and pathologic entities, we also regard them as malignant. As has been indicated in previous publications from our institution, metastasis is a feature of about 10 per cent of bronchial carcinoid tumors. It is our feeling at present that surgical resection is the preferred form of treatment for carcinoid tumors as well as for the other two tumors under discussion.

We should like to emphasize two additional points. First, although the cylindroma may appear to be inoperable by ordinary criteria, very excellent palliation can be obtained by resection, even when tumor must be left behind. The low incidence of vascular invasion probably accounts for the better prognosis associated with this tumor as compared to the prognosis for the usual bronchogenic carcinomas.

Second, although muco-epidermoid tumors and many of the carcinoid tumors are of a low order of malignancy and may be removed adequately by sleeve resection of the bronchus or by more conservative means, the pulmonary sequelae of bronchial obstruction may require more radical resection.

DR. CHAMBERLAIN (Closing).—I would like also to thank the discussers who complimented me by discussing this paper.

I might answer Dr. Jensik's question first by saying that his experience and mine are essentially the same. We did not go into the indications in this 15-minute presentation, but hoarseness is usually a contraindication unless a palliative operation is planned. Of course, on many occasions I have had to perform a biopsy on these people because the x-ray therapist will not treat them unless we have a histologic diagnosis. In some cases, when hoarseness is not the major symptom, I have removed the recurrent laryngeal nerve, as I am sure you have, hoping to cure the patient.

I believe I can answer the other discussers together: Dr. Paulson and Dr. Gibbon. It is interesting to me that they were the ones who called your attention to a cautious approach, since I have recently gone over their published reports in detail. Their resectability rates are higher than the average in this country, so it is not surprising that they should warn you to be cautious Dr Gibbon's paper points out that approximately 50 per cent of his patients have had pericardiectomies, and Dr Paulson's and Dr Shaw's resection rate is up in the 70's, as he pointed out to you

I understood Dr. Johnson's presentation in Boston exactly as he recorded it to you today I am sure that he is as anxious to resect these lesions as any of us

If all of us were to be completely honest with ourselves, we must admit that our ability to resect advanced cases of carcinoma *now* is much greater than it was the day we finished our residencies, and my plea before this Society is to insist in our teaching environs that when we send these young men out into the world that they have with them the technical scope and the technical ability to do an "extended resection" should they encounter the need for it

Now I should like to say a word or two in regard to those cases in which we are forced to leave cancer behind At the beginning of an operation a surgeon does not always know that he is going to leave cancer behind. He may think, "Well, this lesion is completely resectable," and go ahead with the intention of resecting it, even though it is necessary to take the pericardium and the atrial wall, etc However, when the operation is almost completed, it is at that time that he discovers that there is still inaccessible carcinoma I do not like to leave carcinoma behind, but on occasions there is no other solution

Sir Clement Price Thomas kindly sent me a copy of his Tudor Edwards Memorial Lecture just prior to presenting it before the British Thoracic Society in May, 1959 It is of interest that the essence of his presentation was a plea for extended efforts to resect carcinoma of the lung In 306 patients operated upon prior to 1951, his resectability rate was 60 per cent In 268 patients operated upon since 1951, his resectability rate was 75 per cent His published report will show that extended operations for carcinoma of the lung may be performed with encouraging results

For those of you who may return to your respective environs with a more aggressive approach, I would like to read this line to you again "It is not our intent to encourage unguarded aggressiveness in the modern thoracic surgeon."

INSTANTANEOUS BLOOD LOSS DETERMINATION DURING THORACIC SURGERY

Robert Klopstock, M.D., Harry H. LeVeen, M.D.** (by invitation), and P. I. Levitan, M.D.*** (by invitation), Brooklyn, N. Y.*

THE MAGNITUDE and duration of present-day surgery, in general, and of thoracic and cardiovascular surgery, in particular, would not be possible without adequate blood replacement. As magnitude and duration of surgical procedures expand, the volume of operative blood loss increases, necessitating replacement of larger and larger amounts of blood. Anatomic structures dealt with in thoracic and cardiovascular surgery carry the risk of brisk hemorrhage on occasions and the demand of speedy restoration of the circulating blood volume. How then may one best maintain an adequate blood volume and at the same time prevent undertransfusion or circulatory overloading?

The work of Ebert and Stead[1] clearly indicates that during the course of blood loss in normal donors there is no gradual decrease in blood pressure and pulse rate. These authors state, "the onset of collapse was sudden. Until it occurred, the subject had no complaints. In three subjects collapse developed from 1 to 4 minutes after venous suction was completed. The compensatory mechanism appeared to break down suddenly even though no more blood was being removed and the position of the subject had not been changed." This fact is well illustrated by a diagram which has been adapted from Barcroft and others[2] (Fig. 1) to demonstrate the changes in vital signs during the brisk hemorrhage in a normal donor. The blood pressure which starts in the neighborhood of 120 does not fall, the pulse rate rises but little, and yet the cardiac output continuously diminishes. It is only when compensation fails that the blood pressure drops suddenly. This shows that the blood pressure and the pulse rate cannot be relied upon as an index of adequate replacement. Neither the rise in pulse rate nor the fall in systolic pressure makes its appearance until the volume of blood loss is greater than can be compensated for by vasoconstriction. This usually does not occur until after 800 to 1,500 c.c. of blood is lost, if the

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patient is a well nourished and hydrated adult Although venous pressure is of some value in determining the extent of blood loss, it becomes valueless during rapid bleeding and rapid replacement During severe hemorrhage the sudden replacement of blood may fail to bring about a recovery in the hemodynamic alterations even when replacement has been of the proper amount There have been various explanations for this failure of transfusion to prevent the disturbances in hemodynamics, some of which have been ascribed to the high citrate concentration of bank blood The citrate in blood enhances the action of potassium by removing its ionic antagonist, the calcium The potassium concentration of bank blood rises to 25 mEq per liter by the end of 2 weeks The rapid infusion of this bank blood may induce cardiac arrest or a state not unlike that of forward circulatory failure It is under these circumstances that

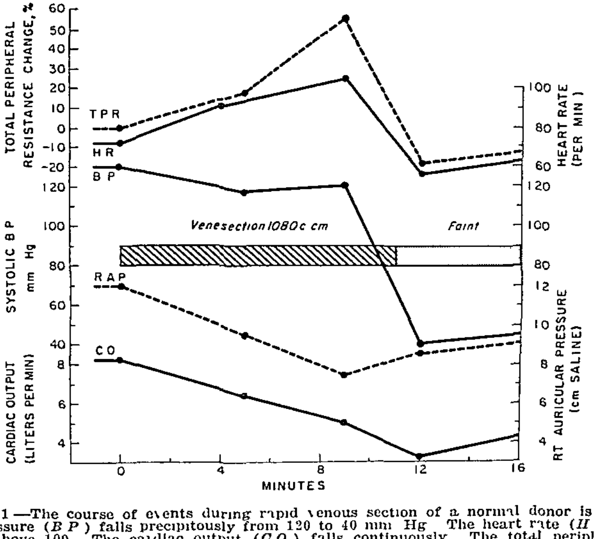

Fig 1 —The course of events during rapid venous section of a normal donor is charted Blood pressure (*B P*) falls precipitously from 120 to 40 mm Hg The heart rate (*H R*) does not rise above 100 The cardiac output (*C O*) falls continuously The total peripheral resistance (*T P R*) rises until decompensation occurs Right auricular pressure (*R A P*) falls continuously during the bleeding

venous pressure will fail to differentiate between overtransfusion and forward circulatory failure induced by high potassium concentration of bank blood It is therefore, obvious that if accidents are to be avoided during surgery entailing massive blood loss that the amount of loss *must be continuously measured* during the operative procedure and exact replacement made for the amount which is lost

Since the first study of blood loss during some of the most common operations was reported by Gatch and Little[3] in 1924, many investigators have made extensive measurements of *operative blood loss in the various fields of surgery* and concluded that volume lost was always greater than the surgeon estimated and that the circulatory volume may be decreased considerably before clinical shock is noted.

Great credit should go to Wangensteen[1] for having suggested (1942) the relatively simple and accurate method for determining operative blood loss *as it occurs* by weighing the dry sponges before and after their use and thus calculating the blood lost during surgery.

In the field of thoracic surgery, White and Buxton,[5] then Miller, Gibbon, and Allbritten,[6] made very valuable studies of blood loss during the various major thoracic procedures. Gibbon[6] and his associates pointed out that they were unable to estimate the amount of blood which had been lost and the amount which should be replaced by observing the vital circulatory signs.

Operative blood loss has previously been determined by both the gravimetric and the colorimetric methods. Blood volume studies were done by the dye dilution method, according to Gibson and Evans,[9] and by radioactive tagging of blood components, and the blood loss has been calculated in these ways. However valuable these methods are, they are not very suitable for the routine and everyday evaluation of blood loss in the operating room when extensive procedures of long duration are carried out.

The possibility of using *the phenomenon of electrical conductivity* in the determination of operative blood loss has been investigated by Harry H. LeVeen.[7]

The conductivity method is based on the fact that blood is a solution of almost constant electrolyte composition. Even in "low salt syndrome" and other more serious disease states, the total sodium does not vary by more than 10 to 20 c.c. mEq. per liter. The extent of blood loss can therefore be assessed by measuring the quantity of lost electrolytes.

The electrical resistance of a solution decreases with increasing electrolyte concentration. More concentrated solutions of electrolyte will allow for greater passage of current according to Ohm's law. If blood is added to water in varying concentrations, a direct proportional relationship between concentration of blood and conductance results. Since small changes in conductance can be accurately measured with a Wheatstone bridge, the change in conductance produced by the addition of blood to known volume of water can be determined precisely. With a suitable Wheatstone bridge and proper temperature compensation, determinations are accurate to 0.5 per cent.

LeVeen,[7] utilizing the discussed principles, carried out extensive preliminary experiments and devised an apparatus, the blood loss monitor, which calculates and instantaneously registers all blood delivered into it.

DESCRIPTION OF THE BLOOD LOSS MONITOR

The apparatus consists of a large stainless steel tub with an agitator which continuously extracts the electrolytes from the sponges and clots. A suction pump transfers blood from the operating table directly into the tub (Fig. 2). This procedure makes possible the addition of blood loss taken up via suction as well as from bloody sponges. Since conductivity increases with increasing temperature of the solution, automatic temperature compensation was accomplished by introducing a thermistor into one arm of the conductivity bridge. The thermistor assumes the temperature of the water in the reservior and changes the resistance of one arm in the bridge to compensate for the decreasing resistance of the solution at increased temperatures. It was desirable to have a direct reading instrument which would obviate the difficulties of manually balancing the conductivity bridge. Hence, a servomechanism was coupled with the conductivity bridge. The servomotor continuously brings the bridge to the null balance point. Instantaneous and continuous detection of conductivity changes are made. The conductivity bridge and cell must be specially constructed to operate on low voltages in order to minimize polarization and, at the same time, maintain its sensitivity. All components of the machine are constructed to meet explosion proof requirements for use in an operating room. The bridge is calibrated in cubic centimeters of blood rather than in solution conductance (the unit of electric conductivity). Blood loss is measured in increments of 100 c.c. up to 8,000 c.c. and with possible estimate of 25 to 30 c.c. within the increment. There is also an arrangement to measure small volume of blood loss from 0 to 800 c.c. to be used in surgery of children. This dial can be read with an accuracy to 20 c.c. and estimated to 10 c.c. within the increment (Fig. 3). This range can be put into operation by turning the proper switch. A centrifugal pump empties the tub following usage and the

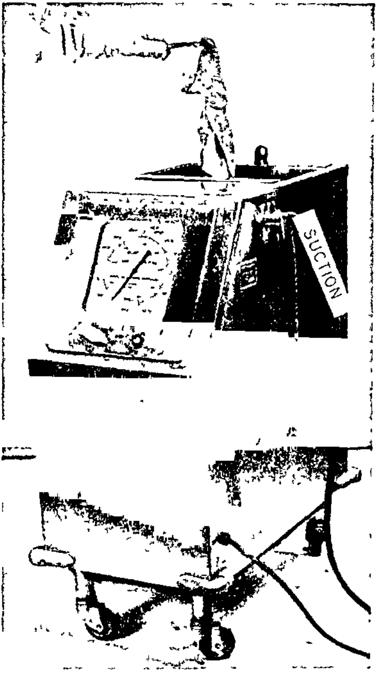

Fig 2 —A photograph of the blood loss monitor is shown in simulated use. The bloody sponges are dropped in the open tub The suction is connected to the side of the apparatus. The dial face can be seen

tub can be rapidly emptied into a regular sink and refilled so that losses greater than 8,000 c.c. can be measured. The machine is cleaned with a chlorinated detergent following use and rinsed with tap water. A stainless steel measure is used to measure the initial quantity of tap water placed in the tub. Fixed resistances with push buttons are included so that the calibration of the machine can be pre-tested before use. A null balance of 0 c.c. of blood is automatically accomplished by using tap water of low conductivity or distilled water. Correction for the initial conductivity of the water is then unnecessary. A schematic drawing of the instrument is shown in Fig. 4.

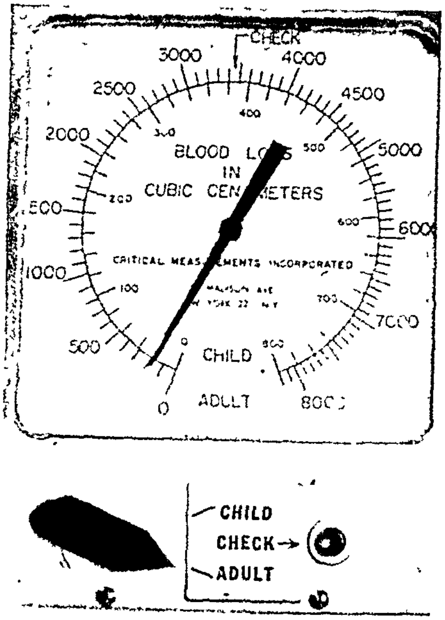

Fig. 3.—The dial face together with the range switch is illustrated in detail. When the switch is in the "adult" position readings are made on the outer circular scale. When the switch is in the "child" position the inner circular scale is used for reading.

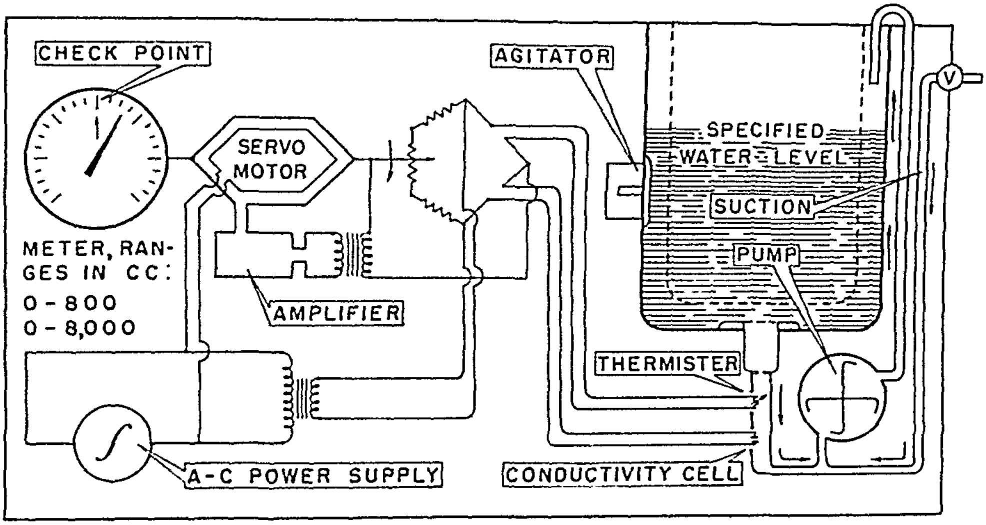

Fig. 1.—Schematic diagram of the automatic blood loss meter. A measured volume of distilled water (25,000 c.c.) is added to the tub. An agitator extracts electrolytes from the sponges, lap pads, and clots. A suction apparatus transfers blood from the operative site to the tub. Automatic temperature compensation is accomplished with a thermistor which forms one arm of this bridge. The conductivity cell is also shown. A servomotor continuously keeps the bridge at the null balance point. The dial of the meter is calibrated directly in cubic centimeters of blood. Sponges and laparotomy pads are held in a stainless steel basket indicated by broken line inside container.

Remarks—It is evident that sodium chloride solutions cannot be used for irrigation purposes or to moisten sponges and pads unless a definite measure of the amount of sodium chloride used is made and subtracted from the final total of indicated blood loss We use a solution of 2 5 per cent glucose for moistening laparotomy pads for irrigation Since glucose is a nonelectrolyte, it does not interfere with the readings

OBSERVATIONS

The blood loss monitor was used in 62 patients who underwent major thoracic and cardiovascular surgery * In Table I, the observed minimum and maximum blood loss values are tabulated for each type of operation and the calculated averages are noted These are approximately equal to those reported by other authors, notably by Miller, Gibbon, and Allbritten Blood loss sustained up to the opening of the pleural cavity ranged 150 to 750 c c with an average of 364 c c It should be stressed that there was no need in any case for additional blood replacement after completion of the surgical procedure if blood replacement was made according to the indication on the monitor In all cases there was less than 1 2 Gm change in the hemoglobin value on the first to the fourth day as compared with preoperative values Thornton and Adams[5] pointed out that the amount of hemoglobin tends to drop postoperatively in those cases where blood replacement has been inadequate This postoperative drop in hemoglobin value described by Thornton and Adams did not occur in our cases in which the blood replacement was carried out under the guidance of the blood loss monitor

There were only 2 cases (No 1 and No 2) in which shock occurred during surgery, and these observations are described fully because of their study value

COMMENT ON ILLUSTRATIVE CASES

In this instance it was decided to compare the accuracy of the anesthetist's clinical estimate to blood loss registered by the monitor Therefore, the "dial indication" of blood lost was unknown to him at the time vital signs had changed

CASE 1—*Lobectomy for Carcinoma With Chest Wall Involvement*—

The patient was a 39 year old man with a round tumor in the right upper lobe On exploration of a carcinoma it appeared that it was anatomically resectable by means of an upper lobe resection, even though the tumor bearing part of the lobe was densely adherent to the parietal pleura in a circumscribed area In addition, the entire upper lobe was attached by vascular adhesions to the parietal pleura Therefore an extrapleural dissection was carried out This patient exhibited an unusual degree of oozing over a prolonged period of time During the procedure, the degree of blood loss was not appreciated by the anesthetist until the vital signs changed At this time 3,500 c c of blood loss was registered *while* only 2,000 c c had been replaced (Fig 5) The known deficit was corrected gradually and the patient's condition returned to normal *Total blood loss and replacement for the* operation was 7,000 c c In the postoperative period, no additional blood replacement was necessary

This observation illustrates the wide discrepancy between clinical impression and accurate measurement of blood loss It is in such cases, when the blood loss is small but continuous, that undertransfusion is common

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*See Addendum

TABLE I. OPERATIVE BLOOD LOSS MEASURED BY MONITOR

TYPE OF SURGERY	NO. OF CASES	MINIMUM	MAXIMUM	AVERAGE		SHOCK		ADDIT. REPLACEMENT 48 HR. POSTOP.	REMARKS
				AUTHOR	MILLER, GIBBON, ALLBRITTEN	DURING OPERATION	48 HOURS POSTOP.		
Miscellaneous chest wall procedures	4	450	3,500	2,200		–	–	–	
Exploratory thoracotomy	9	150	3,000	1,006	1,074	–	–	–	
Pulmonary wedge resection	3	450	950	767		–	–	–	
Segmental resection	14	1,150	2,500	1,812		–	–	–	
Lobectomy	12	950	2,850	1,724	1,778	–	–	–	
Lobectomy (cancer, chest wall)	1	7,000				1*	–	–	*Short duration (considered in detail)
Lobectomy + segment	4	1,500	3,050	2,252		–	–	–	
Pneumonectomy	4	1,650	2,250	1,825	1,915	–	–	–	
Decortication	1		1,400			–	–	–	
Mediastinal tumor	1		1,050			–	–	–	
Mitral commissurotomy	4	950	2,500	1,513		1†	–	–	†Short duration (considered in detail)
Esophageal surgery	3	1,700	2,650	2,105	1,876	–	–	–	
Pericardectomy	1		1,050			–	–	–	
Resection of aneurysm of thoracic aorta with hypothermia	1	6,200				–	–	–	(considered in detail)
Total	62								
On entering pleural cavity	58	150	750	364					

Less than 1.2 Gm. change in hemoglobin for all cases, 1 to 4 days postoperative as compared to preoperative values.
*Case 1.
†Case 2.

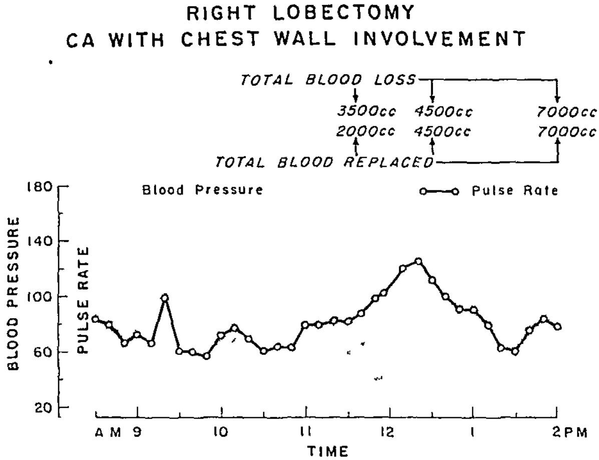

Fig 5.—Illustrates not only the ease of management of a patient who during surgery had gradual blood loss of 7,000 c c with change in the hemodynamics but also the facility with which known large deficits can be readily corrected

Case 2 —*Mitral Commissurotomy* —

The patient was a 37 year old white man with mitral stenosis During the otherwise uneventful procedure there was a sudden loss of 1,200 c c of blood following tear of the left atrium and superior pulmonary vein Blood pressure was unobtainable for a short period of time, but returned to normal after replacement of the indicated volume The patient did well following surgery and no further blood replacement was needed (Fig 6)

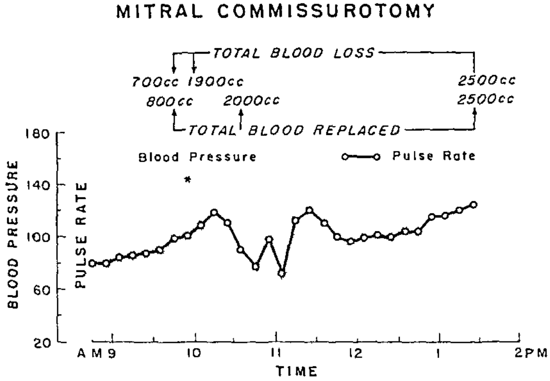

Fig 6 —Brisk blood loss precipitating shock during cardiac surgery is easily managed by monitoring and replacing the blood loss as it occurs

When blood loss is sudden and massive one may "get lost" in the management of replacement if it is based on clinical estimate. It is in such cases that overtransfusion, most commonly, and cardiac arrest, occasionally, are induced.

The train of events substantiates also the experimental data on normal donors which indicate that vital signs do not change until considerable blood has been lost and only then they change suddenly.

Hypothermia.—

The increasing use of hypothermia poses problems for both surgeon and anesthesiologist. Not only does hypothermia render the vital signs valueless, but it also enhances the tendency toward cardiac arrest. During hypothermia, patients tolerate blood loss very poorly and the blood volume is restored very slowly after hemorrhage. This is partly brought about by a fall in the osmotic pressure of the plasma protein during hypothermia. Under these circumstances fluid cannot be rapidly mobilized from the tissue spaces. The instantaneous determination of blood loss was of considerable aid not only in thoracic surgery, but in all surgery performed with hypothermia.

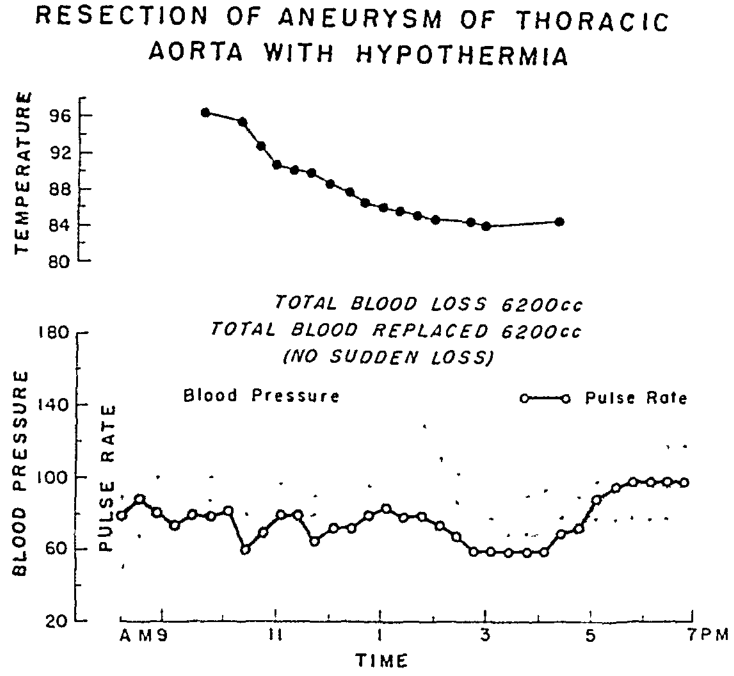

Fig. 7.—Monitored blood loss and replacement during 10-hour hypothermic vascular surgery is graphically shown.

The following case report illustrates the usefulness of monitored blood loss in cardiovascular surgery carried out under hypothermia with necessarily hypotensive blood pressure levels and altered pulse rate.

Case 3.—*Excision and Replacement of Descending Thoracic Aorta.*—

The patient was a 42-year-old white man with a large fusiform aneurysm of the descending thoracic aorta. At exploration the dilatation was found to extend from just distal to the left subclavian artery to a point just above the diaphragm. Under hypothermia a

Teflon prosthesis was used to bypass the aneurysm which was then resected; the prosthesis was left as a permanent bypass. There was no dramatic blood loss during the 10 hour procedure, but after replacing the volumes of blood indicated by the monitor, it was found that 6,200 c.c. of blood had been lost by continual ooze. The patient had an uneventful postoperative course and no further blood replacement was necessary (Fig. 7).

In the properly monitered case, blood deficit and overtransfusion do not occur if loss and replacement are checked periodically during the course of prolonged surgery. Hourly check should be considered the minimum interval during the uneventful progress of an operation. A typical chart of monitored blood loss is shown in Fig. 8.

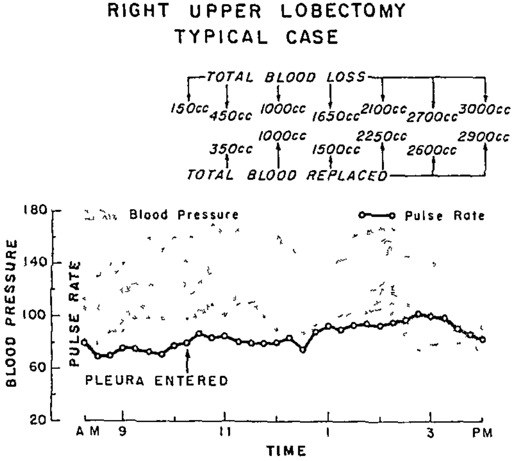

Fig 8.—The matching of blood replacement to blood loss is shown in a typical intrathoracic surgical procedure

GENERAL COMMENTS

In the foregoing, data are presented to document the value of an apparatus, the blood loss monitor, for accurate determination of blood loss during surgery as it occurs. The construction and function of the apparatus is based on the fact that the blood is a solution of almost constant electrolyte composition. The extent of the blood loss is assessed by measuring the quantity of lost electrolytes.

Since the characteristics of blood as an electrolyte are utilized as a measurement of blood, all the factors affecting conductivity in blood must be reckoned with.

Nonelectrolyte in high enough concentration will effect a reduction in conductivity. The usual concentration of glucose and nonprotein nitrogen in blood do not produce a perceptible change. Serum protein and hemoglobin do influence conductivity in an ideal way. For [illegible] am per [illegible] protein, conductivity increases approximately 2 per cent. A blood loss of 100 c.c. in a patient with a gram per cent deficit in plasma protein would appear as a loss of 102 c.c. This would cause the patient to be overtransfused by 2 per cent. A change in hematocrit from 50 to 5 will register approximately 20 per cent increase in loss. An anemia of 50 per cent would bring about an over-replacement of blood loss by an amount slightly in excess of 10 per cent. The method makes moderate corrections for severe hypoproteinemia and anemia.

Open Heart Surgery.—We have not yet had the opportunity to use the blood loss monitor in open heart surgery, but it seems apparent that such an apparatus could be of inestimable value.

The accurate determination of the blood lost before the perfusion begins could be accomplished with ease. During perfusion all blood lost from the oxygenator-patient-circuit must be accurately known so that correct volume of blood may be maintained in the patient and the perfusion terminated with the patient in normovolemic state. In infants, of course, this assumes even greater importance since small amounts of blood represent larger proportions of total blood volume.

Rapid losses of large quantities of blood during cannulation as occurs on occasion, or accidental injury to major vessels in the preparation for perfusion, may prejudice the outcome if fast and accurate replacement is not carried out prior to the total body bypass.

Compensated Hypovolemia.—In considering the efforts to safeguard the surgical patient against the hemodynamic changes brought about by over- or undertransfusion, attention should be directed to the possible danger inherent in compensated hypovolemia. Recent experiment of ours had shown that potassium excretion is impaired in compensated hypovolemia even though blood pressure and pulse rates remain unchanged. During compensated hypovolemia in animals, serum potassium levels will rise with infusions of hyperkalemic blood (bank blood). This rise does not occur in normovolemic animals. The rise of serum potassium exposes the animals to the possibility of cardiac arrest. These experimental observations confirm the effort that blood loss be replaced quantitatively as it is lost.

In Conclusion.—The feeling is expressed that the instantaneous and continuous determination of operative blood loss gives the surgeon the assurance that the patient's hemodynamics will not undergo sudden collapse and that the patient will not be exposed to biochemical changes making him susceptible to cardiac arrest because an exact replacement is made as blood is lost. The maintenance of hemodynamic equilibrium enhances greatly the execution of the purpose of surgery and safeguards the patient from measures which are necessitated under the duress of hemorrhage.

SUMMARY

Instantaneous and continuous determination of operative blood loss was carried out in 62 major thoracic procedures utilizing an apparatus, the blood loss monitor, based on the principle of electrical conductivity of the blood.

Results are tabulated

Pathophysiology of response to blood loss has been discussed

The method proved to be simple, reliable, accurate, and extremely useful

ADDENDUM

Since this report was submitted, the blood loss monitor was used in 57 additional *major thoracic and cardiac operations In none of the patients did shock occur during* or after the completion of surgery, and in no instance was it necessary to use additional *blood replacement beyond the amount indicated by the monitor during the surgical* procedure

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DISCUSSION

DR KLOPSTOCK—*In closing, I would like to show a short* motion picture to demonstrate the blood loss monitor in simulated action Here you see the apparatus with the dial face registering blood loss up to 8,000 c c Before using, 0 point is being tested Now 1,000 c c *of blood is delivered into the tub, watching the dial you see that it instantly registers* 1,000 c c Then the content of the suction bottle, containing 150 c c of blood, is suctioned into the tub and you can notice that the registered total is now 1,150 c c Bloody sponges and pads are *now dropped into the tub, registering an additional 200 c c—altogether 1,650 c c* of blood loss Excessive foam formation in the tub solution is prevented by addition of an antifoam agent Thank you

USE OF A MECHANICAL RESPIRATOR IN THE MANAGEMENT OF RESPIRATORY INSUFFICIENCY FOLLOWING TRAUMA OR OPERATION FOR CARDIAC OR PULMONARY DISEASE

Frank C. Spencer, M.D., Donald W. Benson, M.D. (by invitation), W. C. Liu, M.D. (by invitation), and Henry T. Bahnson, M.D., Baltimore, Md.*

THE USE of a mechanical respirator to maintain patients with severe pulmonary insufficiency through the critical period after pulmonary resection was first described by Björk and Engström in 1955.[1] Subsequent experience has shown the validity of their premise, that a satisfactory recovery is possible if the patient can be helped to survive the critical early period after operation when respiratory function is poor because of trauma to the lung, increased secretions, pain, and fatigue. Avery, Mörch, and Benson[2] have used a respirator to relieve respiratory insufficiency resulting from a flail chest after crushing injuries, the respirator being used in some instances until the rib cage became stable enough to prevent embarrassing paradoxical breathing. In 1957, Björk and Engström[3] had used the respirator in 61 patients, including 3 in pulmonary edema, and mentioned in an addendum the use on patients following cardiopulmonary bypass and open heart surgery.

We wish to emphasize the value of a respirator after open heart surgery to carry some patients through the early postoperative period when survival is not possible without this supportive measure. In the cases to be reported, respiratory insufficiency followed trauma in 1 case, pulmonary surgery in 2, and cardiopulmonary bypass and open correction of cardiac defects in 7.

THE RESPIRATOR

The Mörch respirator used in this group of patients consists of a piston, the stroke of which can be varied from 0 to 3.2 liters by changing the radius on a crank. The crank in turn is driven by an electric motor with a variable speed reduction unit which allows regulation of the rate from 0 to 40 strokes per minute. The stroke volume and cycling rate are the only adjustable factors. Air is pulled into a chamber through a one-way valve by the backward movement of the piston and is then pushed out by the forward movement through

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*Dr. Spencer is a John and Mary R. Markle Scholar.

a humidifier to a valve placed as close to the patient as possible During the inspiratory stroke, air is forced through this valve to the patient When the respirator is filling, the same valve allows passive exhalation by the patient to the atmosphere and at the same time stops aspiration of the patient's expired air into the apparatus The respirator has been previously described,[2] and a diagram is shown in Fig 1

This apparatus has the advantages of a large stroke volume and simplicity of management The large and certain stroke volume allows one to hyperventilate almost any patient sufficiently to produce slight hypocapnia and alkalosis and thus control the ventilation without resistance from the patient

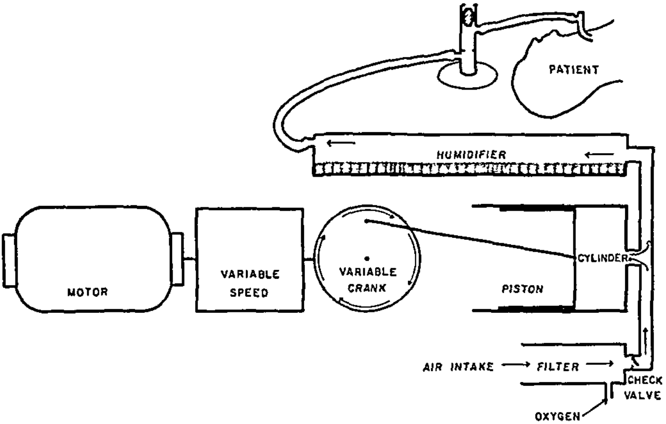

Fig 1—A diagram of the construction of the respirator is shown The valve is placed as close to the tracheotomy tube as possible

In addition, a loose tracheotomy tube can be used with the large stroke so that pressure necrosis does not occur and secretions can be blown up around the tube A precise regulation of stroke volume is not needed as excess volume is simply blown past the loose tube In practice, stroke volume and rate are initially increased to produce apnea and then reduced to a point just above that at which the patient makes respiratory effort At this level of ventilation, arterial pH is usually mildly alkalotic (pH 7 45 to 7 60) Rate and stroke are subsequently altered to match the patient's demands and to maintain mild hypocapnia and alkalosis

Humidification to prevent drying of the tracheal mucosa is an important consideration with the large volume of gas used The respirator is equipped with a humidifier but this was supplemented by instilling 5 ml of sterile saline into the tracheotomy tube every 30 minutes and, in some instances, by connecting an intravenous saline drip to the tube near the patient and running this slowly Inadequate humidification was probably the cause of t' [illegible] th reported in this group of patients (Case 4, T [illegible] S [illegible]

TABLE 1

CASE NO.	NAME, AGE, SEX	DIAGNOSIS	HISTORY OF:		PULMONARY ARTERY PRESSURE (mm. Hg)	OPERATION	INDICATIONS FOR USE OF RESPIRATOR	POST-OPERATIVE DAY RESPIRATOR BEGUN	DAYS RESPIRATOR USED	RESULT
			DYSPNEA	CONGESTIVE HEART FAILURE						
Case 1	E. P. 34, F	Atrial septal defect with pulmonary hypertension	Moderate; 12 months	Moderate; 6 months	80/26	Closure; atrial defect	Hypotension and acidosis (pH 7.15)	2	4	Recovery
Case 2	G. L. 14, M	Ventricular septal defect with pulmonary hypertension	Minimal	No	90 systolic	Closure; ventricular defect	Hypotension and dyspnea	2	1	Recovery
Case 3	V. C. 21, F	Tetralogy of Fallot	Moderate	No	—	Correction of tetralogy of Fallot	Dyspnea, anoxemia, low cardiac output	2	6	Recovery
Case 4	B. B. 19, F	Tetralogy of Fallot	Marked	No	—	Correction of tetralogy of Fallot	Dyspnea, hypotension and acidosis	1	11	Died from pneumonia
Case 5	J. F. 37, M	Mitral insufficiency	Severe	Severe	53/36	Repair; mitral insufficiency	Severe dyspnea	7	3	Recovery
Case 6	A. R. 54, F	Mitral stenosis	Severe	Severe	61/28	Mitral valvulotomy	Severe dyspnea	7	5	Recovery
Case 7	V. G. 43, F	Mitral stenosis, postoperative hemiplegia	Severe	Severe	50 (mean)	Mitral valvulotomy	Dyspnea, hypotension, and coma	1	43	Recovery
Case 8	B. L. 56, M	"Flail" chest from multiple rib fractures	Severe	No	—	—	Dyspnea, acidosis	1	21	Recovery
Case 9	A. H. 54, M	Herniation of heart following pneumonectomy	No	No	—	Radical right pneumonectomy	Hypotension and dyspnea with cardiac herniation into right pleural cavity	2	4	Recovery
Case 10	C. W. 44, F	Fibrothorax with pulmonary insufficiency, decortication	Severe	Mild	90/27	Decortication, left lung	Dyspnea, coma, and hypotension	3	41	Recovery

diffuse tracheobronchitis, however, and the possibility cannot be excluded that a pneumonia was the initial factor requiring aid from the respirator.

A possible disadvantage of a positive pressure respirator is the harmful effect on cardiac output. Studies by Cathcart and associates,[4] confirmed by work of Maloney,[5] and of Cournand and associates[6] have shown a progressive decrease in cardiac output as the mean endotracheal pressure is increased. We did not recognize any significant changes in cardiac output in the patients reported here when the respirator was used as described. Cardiac output was measured in 2 patients (Cases 3 and 4, Table I) and was not found to change significantly when the respirator was started. In 3 other patients not included in this series, no significant changes in cardiac output occurred with the use of the respirator. The necessity for a tracheotomy when the respirator is used is not a significant disadvantage. Most patients with a degree of pulmonary insufficiency sufficient to require a respirator are unable to remove bronchial secretions properly, so a tracheotomy is required for this reason alone.

CASE REPORTS

The 10 cases in which the respirator was used are listed in Table I. The 7 patients with cardiac disease included 1 patient with an atrial septal defect and severe pulmonary hypertension, 1 with a ventricular septal defect and moderate pulmonary hypertension, 2 patients with tetralogy of Fallot, and 3 with disease of the mitral valve, all 3 of whom had moderate pulmonary hypertension. The other 3 cases included 1 with a flail chest from multiple rib fractures, 1 with repeated herniation of the heart into the right pleural cavity after a radical pneumonectomy, and 1 with respiratory insufficiency from a fibrothorax of 13 years' duration. The respirator was used for intervals from 1 to 42 days. All but one recovered.

CASE 1.—E. P., a 34 year old woman, had dyspnea and ankle edema for 1 year. Cardiac catheterization showed an atrial septal defect with a pulmonary artery pressure of 80/28 mm. Hg. The pulmonary blood flow was 1.6 times the systemic, and pulmonary arterial blood was 79 per cent saturated; pulmonary vascular resistance was 0.38 of the systemic resistance. The atrial defect was sutured during cardiopulmonary bypass on Feb. 1, 1958, through a right intercostal incision. Her course is charted in Fig. 2. Although her immediate postoperative condition was satisfactory (systolic blood pressure 100 mm. Hg, arterial blood pH 7.44, blood volume 80 ml. per kilogram), a progressive hypotension and vasoconstriction developed in the next 18 hours with a severe metabolic acidosis. Twelve grams of sodium bicarbonate were given intravenously for blood pH values as low as 7.15. An infusion of norepinephrine was used to maintain the systolic blood pressure at 90 mm. Hg. The patient became comatose and increasingly dyspneic, although there was no cyanosis and the chest roentgenogram showed no gross abnormality. She appeared in extremis 20 hours after operation. As a last resort, tracheotomy was done and the respirator connected when the arterial pH was 7.22. Her condition promptly improved with the respirator, the pH rising to 7.28 and then to 7.60 12 hours later. The vasopressor drug was gradually stopped over the next 18 hours as the patient's condition steadily improved. The respirator was gradually stopped over the fourth and fifth postoperative days and subsequent convalescence was uneventful.

Comment. *Severe hypotension and metabolic acidosis subsided with the use of a respirator in a patient with increased pulmonary resistance and an atrial septal defect.*

CASE 2.—G. L., aged 14, had repeated respiratory infections and growth retardation from a ventricular septal defect but had no dyspnea or congestive failure. The pulmonary artery systolic pressure was 90 mm. Hg and the pulmonary blood flow 11 L. per minute. On Aug. 21, 1957, the ventricular septal defect was sutured during cardiopulmonary bypass through a bilateral anterior thoracotomy. The pulmonary artery systolic pressure fell with closure of the defect from 80 to 53 mm. Hg. Twelve hours after operation, an acute hypotension began that soon was associated with a serum sodium of 125 mEq. per liter and hemoconcentration with an hematocrit of 54. The hypotension was refractory to vasopressor drugs but responded to hypertonic saline. Progressive dyspnea on the second postoperative day was not relieved by a tracheotomy, so the Mörch respirator was begun 4 hours later. Dyspnea was promptly relieved, and the hypotension improved. The pH 3 hours later was 7.58. He improved rapidly and within 12 hours the respirator and vasopressor were stopped. He remained in moderate congestive failure with elevated venous pressure and hepatomegaly for the next several days but gradually improved and was discharged in good condition on the twentieth postoperative day.

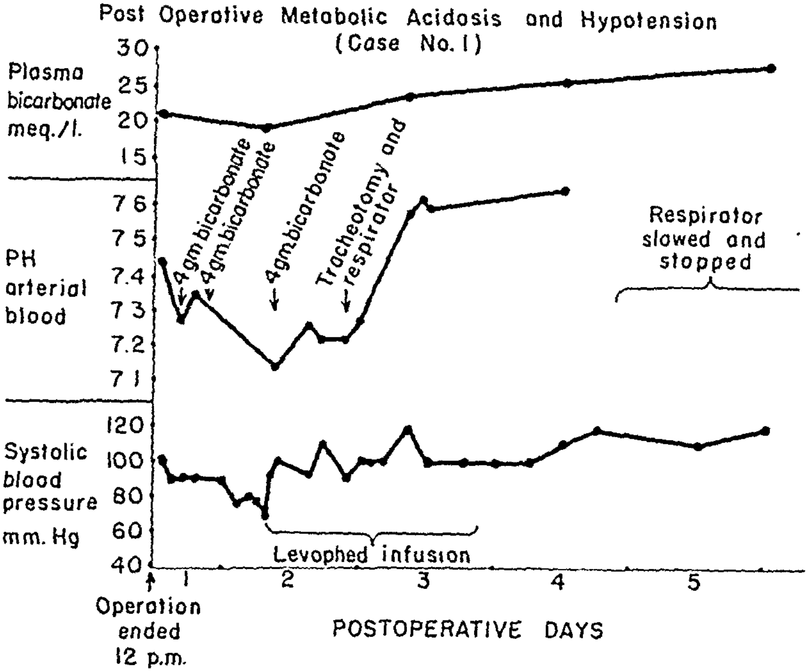

Fig. 2.—The response of postoperative hypotension and metabolic acidosis in Case 1 to a respirator is shown.

Comment: Hypotension and dyspnea, probably from cardiac failure, responded promptly to the use of the respirator after repair of a ventricular septal defect.

CASE 3.—V. C., aged 21, had moderate dyspnea from a tetralogy of Fallot with cyanosis and an hematocrit of 50 per cent. The ventricular septal defect was closed and an infundibular stenosis excised on Oct. 15, 1958, with cardiopulmonary bypass and a median sternotomy. The right ventricular systolic pressure fell from 90 to 30 mm. Hg. Her postoperative course is charted in Fig. 3. Progessive dyspnea and hypotension gradually developed over the next 8 hours. Cardiac output was estimated at intervals from oxygen consumption and blood samples obtained through small plastic catheters in the pulmonary and femoral arteries; this showed a striking reduction of cardiac index, 1.5 L. per minute 8 hours after operation, with an arterial oxygen saturation of 94 per cent. The arterial oxygen saturation subsequently decreased to 82 per cent in spite of an oxygen tent. A tracheotomy was done 12 hours after operation with a rise in oxygen saturation to 88 per cent; dyspnea remained, however, and the Mörch respirator was started at this time. The arterial oxygen saturation rose to 93 per cent and her condition steadily improved. Several hours later the cardiac index had risen to 2.8 L. per minute and the arterial oxygen saturation was 96 per cent. Throughout this period the pH of the arterial blood ranged from 7.36 to 7.58. The respirator was gradually stopped on the sixth and seventh postoperative days and her subsequent convalescence was uneventful.

Comment: The cause of the low cardiac output, anoxemia, and ventilatory insufficiency is unknown in this patient with a tetralogy of Fallot. The response to the respirator was prompt and sustained.

CASE 4.—B. B., a 19-year-old girl, had marked limitation from a tetralogy of Fallot with dyspnea, cyanosis, and an hematocrit of 74 per cent. A left subclavian-pulmonary artery anastomosis had been performed in 1945. On Nov. 7, 1958, the ventricular septal defect was closed, the infundibular stenosis excised, and the subclavian-pulmonary anastomosis closed through a median sternotomy and with cardiopulmonary bypass. The right ventricular systolic pressure decreased from 145 to 32 mm. Hg. Six hours after operation the blood pressure was 70/50 mm. Hg; she was dyspneic and slightly acidotic (pH 7.31). A tracheotomy was done and the respirator begun. Dyspnea was satisfactorily controlled by the respirator, but throughout the remainder of her hospital course she was unable to ventilate satisfactorily without it. Samples of mixed venous blood obtained through a small plastic catheter left in the pulmonary artery at the time of thoracotomy showed a low oxygen content, indicating a low cardiac output. This persisted and never reached a normal level. After the seventh postoperative day, resistance to ventilation progressively increased; bronchial secretions were profuse, purulent, and removed with difficulty. Several episodes of acute ventilatory obstruction were relieved by vigorous suctioning and by bronchoscopy on one occasion. The episodes of respiratory obstruction progressively increased in severity and the patient died on the eleventh postoperative day. Autopsy showed diffuse purulent tracheobronchitis with pneumonia involving all lobes of both lungs.

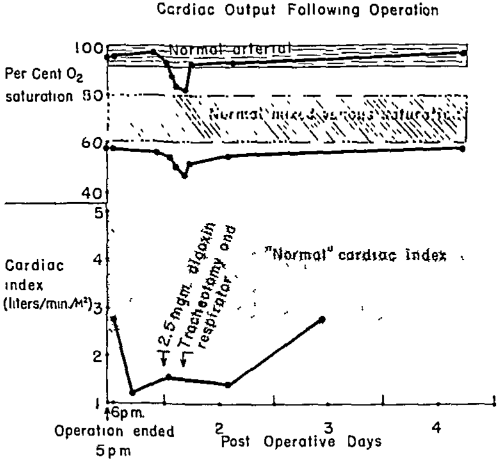

Fig. 3—The response of postoperative anoxemia and low cardiac output in Case 3 to a respirator is shown.

Comment: Dyspnea, hypotension, and metabolic acidosis were present soon after correction of the tetralogy of Fallot. Respiratory insufficiency required the constant use of the respirator for 11 days before the patient died of a diffuse tracheobronchitis.

Case 5.—J. F., aged 37, had mitral insufficiency with severe congestive heart failure, hepatomegaly, and pedal edema. Cardiac catheterization showed a pulmonary artery pressure of 53/36 mm. Hg and a left atrial pressure of 50/20 mm. Hg. The mitral valve was repaired with cardiopulmonary bypass through a right thoracotomy on Dec. 22, 1958. The insufficiency came from two perforations in the aortic leaflet of the mitral valve, probably a result of bacterial endocarditis. After the perforations were sutured, the mitral valve seemed competent; subsequent left atrial pressures were 10 to 15 mm. Hg. Re-operation was necessary on the third postoperative day because of persistent bleeding from a lacerated internal mammary vein. Following the second thoracotomy, dyspnea progressively increased in severity. Bronchial secretions were profuse with numerous râles throughout the chest. The patient became disoriented, with a blood urea nitrogen above 40 mg. per cent. A tracheotomy on the seventh postoperative day resulted in some improvement; the arterial blood pH after tracheotomy was 7.30. Severe dyspnea remained, however, and several hours later the respirator was begun. This promptly controlled the dyspnea and his condition became stable. The serum bicarbonate was 32 mEq. per liter 8 hours after the respirator was started and fell to 27 mEq. per liter 24 hours later. The respirator was used for 3 days, after which it was gradually stopped over a 24-hour period. The patient was discharged in good condition on the twenty-eighth postoperative day.

Comment: Cardiac failure, profuse bronchial secretions, and fatigue resulted in marked dyspnea, respiratory acidosis, and azotemia which were controlled by the use of the respirator for 3 days.

Case 6.—A. R., a 54-year-old woman, had mitral stenosis and insufficiency with dyspnea, hepatomegaly, and ankle edema. She had spontaneously recovered from a massive arterial embolus to the lower extremities 1 year earlier, but femoral pulses were not palpable and bilateral intermittent claudication was present. Cardiac catheterization showed a pulmonary artery pressure of 61/28 mm. Hg and a left atrial pressure of 26/17 mm. Hg; the end diastolic gradient across the mitral valves was 5 mm. Hg. Because mitral insufficiency was considered the dominant defect and also because of the previous arterial embolism she was operated upon through a right posterolateral incision with cardiopulmonary bypass on May 2, 1958. A stenosed mitral valve, less than 1 cm. in diameter, was found in which there was little insufficiency. Both commissures were split to produce an opening over 2 cm. in diameter with little change in the regurgitation. A thrombus was removed from the left atrial appendage and the appendage closed from within the left atrium. The left atrial systolic pressure remained in the range of 25 to 30 mm. Hg after operation. Cardiac failure became progressively more severe in the first few days after operation. On the second postoperative day, the arterial blood pH was 7.36 and the plasma bicarbonate 26 mEq. per liter (Table II). On the fourth postoperative day dyspnea was more severe, with episodes of mental

TABLE II. CASE 6. BLOOD CHEMICAL CHANGES

POSTOPERATIVE DAY	ARTERIAL pH	SERUM BICARBONATE (mEq./L.)	BLOOD UREA NITROGEN (mg. %)
1	7.41; 7.34	27	30
2	7.36	26	32
4		28	50
7		31	64
Respirator begun			
4 hours later	7.58		
10 hours later	7.60		
8	7.7; 7.57	33	
9		31	26

confusion, plasma bicarbonate was 28 mEq. per liter. On the seventh postoperative day dyspnea was so extreme that the patient was comatose with ineffective gasping respiration, a plasma bicarbonate was 31 mEq per liter and blood urea nitrogen was 64 mg. per cent. A tracheotomy was done and the Morch respirator begun. Ten hours later, the pH of arterial blood was 7.6, the following day the pH was 7.7 and subsequently 7.57, plasma bicarbonate was 33 mEq per liter. Forty-eight hours after the respirator was begun the patient was alert and responsive, the urea nitrogen had fallen to 26 mg. per cent. The respirator was gradually stopped between the ninth and the eleventh postoperative days and the patient was discharged in good condition on the twenty-eighth postoperative day.

Comment: Cardiac and respiratory failure, resulting in coma, respiratory acidosis, and azotemia, were controlled with the use of the respirator for 4 days. An earlier use of the respirator was probably indicated.

CASE 7.—V. G., a 43-year-old woman, had progressive cardiac failure from mitral valve disease with dyspnea, hepatomegaly, and ankle edema. Mitral insufficiency was thought to be the predominant lesion. On Feb. 28, 1958, through a right anterolateral incision, cardiopulmonary bypass was used to allow visual examination of the mitral valve. The initial diagnosis proved to be incorrect, however, as severe mitral stenosis was found with a valve opening only 5 to 6 mm. in diameter. Tricuspid insufficiency was present but no mitral insufficiency. A satisfactory commissurotomy was performed which produced minimal regurgitation. A large thrombus was removed from one of the pulmonary veins during the procedure.

A left hemiplegia was noted on recovery from anesthesia, and ventilation was inadequate. A tracheotomy was done and the Morch respirator applied. The first 3 days after operation were characterized by coma, hypotension, elevated venous pressure, and oliguria; vasopressor drugs were used for 48 hours. The arterial blood pH ranged from 7.43 to 7.57 in the first 4 days, and the arterial oxygen saturation 3 days after operation was 99 per cent.

The patient remained comatose with severe cardiac failure for several weeks. The liver was enlarged below the umbilicus and peripheral edema was present. Attempts to stop the respirator resulted in marked cyanosis and dyspnea until 38 days after operation. She was subsequently taken off the respirator for an increasingly longer period until it was stopped completely on the forty-third day. Gradual improvement of the hemiplegia occurred and when she was discharged from the hospital 2 months after operation she was able to walk and had partial use of her left arm.

Comment: Respiratory insufficiency resulting from cardiac failure and hemiplegia would surely have been fatal without the prolonged use of the respirator.

CASE 8.—B. L., age 56, was hospitalized on Dec. 11, 1956, following a crushing injury to the chest in an automobile accident. All 12 ribs in the left hemithorax were fractured, and the first, eighth, and ninth ribs in the right (Fig. 4). Moderate subcutaneous emphysema was present but no pneumothorax. Only a moderate instability of the chest wall was present, but the patient gradually became more and more dyspneic. His subsequent course is charted in Fig. 5. A tracheotomy 12 hours after admission did not relieve the dyspnea. Analysis of arterial blood showed a pH of 7.15, an oxygen saturation of 77 per cent, and a carbon dioxide content of 51 volumes per cent. Artificial respiration was begun with the Morch respirator with rapid improvement in the patient's color and general condition. Twenty-four hours later the arterial blood pH was 7.55, the carbon dioxide content 47 volumes per cent and the oxygen saturation 94 per cent. Subsequent determinations were within normal limits. The respirator was gradually stopped from the fourteenth to the twenty-first day following the injury, and the patient was discharged in good condition 30 days following injury (Fig. 6).

Comment: Severe respiratory insufficiency from a flail chest was not relieved by tracheotomy but was promptly controlled with the respirator.

Case 9.—A. H., age 54, had a radical right pneumonectomy on Sept. 3, 1958, for a large bronchogenic carcinoma. A large amount of pericardium was removed and the pericardial sac left in communication with the right pleural cavity. Two additional thoracotomies were required in the next 24 hours for shock resulting from herniation of the heart into the right pleural cavity. This herniation was precipitated by periods of dyspnea and restlessness during which time the patient would not remain on his left side as prescribed. After the herniated heart had been replaced the third time, a tracheotomy was performed and the Mörch respirator begun. The respirator controlled the dyspnea and restlessness, and it was possible to keep him comfortably on his left side for 4 days, after which the respirator was stopped and further respiratory insufficiency did not occur.

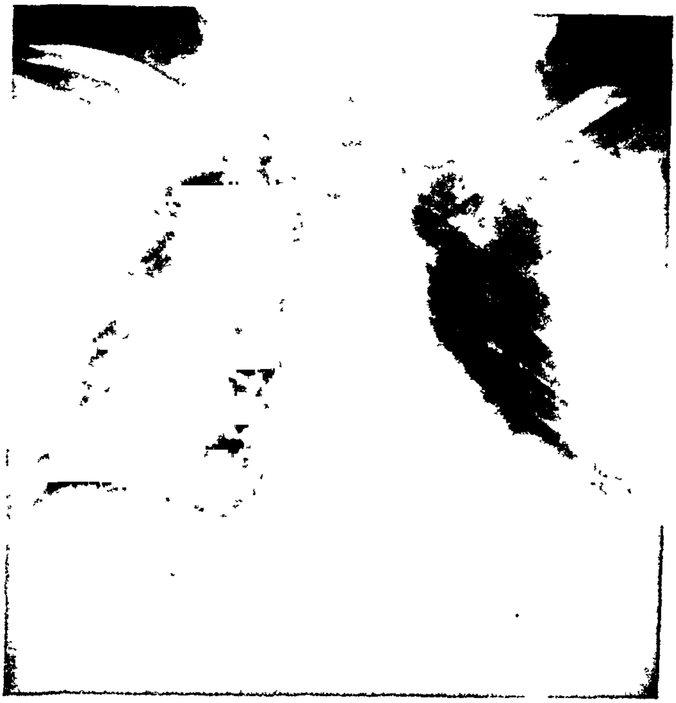

Fig. 4.—Chest roentgenogram following trauma in Case 8. All twelve ribs in the left chest are fractured, as well as ribs 1, 8, and 9 on the right.

Comment: Dyspnea and hypotension in this patient prevented proper positioning to avoid herniation of the heart until respirations were controlled with a respirator.

Case 10.—C. W., age 44, had severe respiratory insufficiency from a fibrothorax which followed pneumothorax therapy for tuberculosis 13 years before. She was totally incapacitated with dyspnea and moderate right heart failure. The vital capacity was 1,400 ml., the maximum breathing capacity 51 L. per minute, the arterial oxygen saturation 80 per cent, and the pulmonary artery systolic pressure 90 mm. Hg. After many preoperative studies and much deliberation, a decortication was undertaken on Mar. 15, 1957. A complete decortication was possible, but a massive hemothorax caused increasing respiratory insufficiency over the next 48 hours. At this time the patient almost died in acute respiratory failure, but she was resuscitated with an emergency tracheotomy, evacuation of the hemothorax, and maintenance of the respirations with a respirator. After the respirator had been

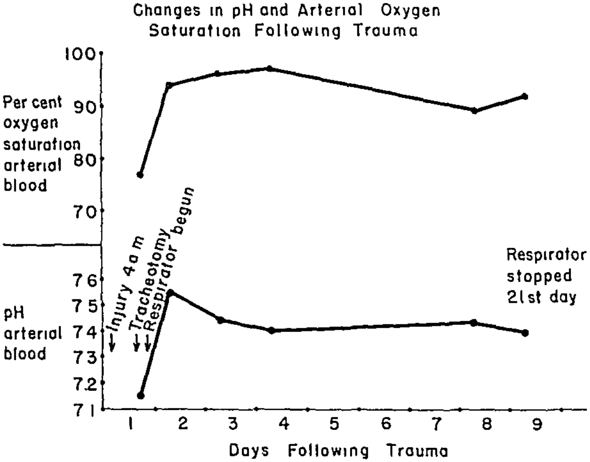

Fig 5—The response to a respirator of anoxemia and respiratory acidosis caused by a flail chest in Case 8 is shown The response to tracheotomy without a respirator was not satisfactory

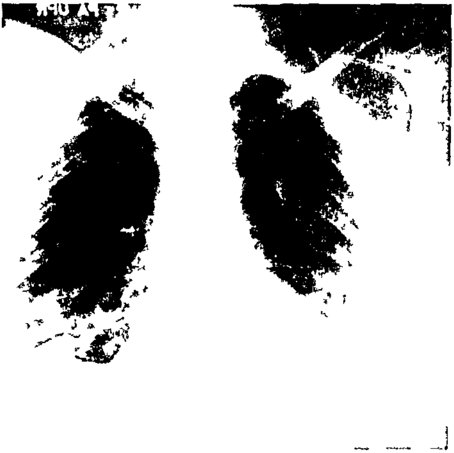

Fig 6—Chest roentgenogram 18 days following injury in Case 8 The subcutaneous emphysema has subsided the respirator was stopped on the twenty first day

used for 48 hours the arterial oxygen saturation was 85 per cent, the pCO_2 40 mm. Hg, and the pH 7.28. Attempts to stop the respirator over subsequent days resulted in severe dyspnea and cyanosis with arterial oxygen saturations of 30 to 45 per cent. The respirator was constantly required for 5 weeks, after which it was gradually stopped by the forty-first postoperative day. When discharged from the hospital 2½ months after operation, oxygen saturation was only 75 per cent, pCO_2 35 mm. Hg, and the pH 7.42. The patient's exercise tolerance steadily improved, however, and 6 months later she was able to walk 18 blocks with no dyspnea whatever.

Comment: Because of severe respiratory insufficiency, a respirator was needed for this patient for 6 weeks following decortication of a long-standing fibrothorax.

DISCUSSION

Etiology of Respiratory Insufficiency.—The respiratory insufficiency in the 3 patients with pulmonary disease (Cases 8, 9, and 10, Table I), was caused by the mechanical effects of the disease present—a flail chest, a pneumonectomy and cardiac herniation, and a chronic fibrothorax, respectively. The cause of the insufficiency is less obvious, however, in the 7 patients with cardiac disease. Cardiac failure, pulmonary hypertension, and temporary decrease in pulmonary function from thoracotomy are possible causative factors. Patients with chronic cardiac failure, which was present in 3 patients with mitral valve disease (Cases 5, 6, and 7, Table I), often have severe cardiac failure after mitral commissurotomy. This tendency is well shown by the stormy, and often fatal, postoperative course following digital commissurotomy for mitral stenosis in patients with intractable congestive failure (so-called Class 4 patients).[7]

Pulmonary hypertension, which was present in 5 of the 7 patients, is also often associated with postoperative difficulties with ventilation and hypotension. These difficulties may arise from the fact that anoxia markedly increases pulmonary vascular resistance. A degree of anoxia easily tolerated by a patient whose pulmonary artery pressure is normal may be disastrous to the patient with severe pulmonary hypertension.

The cause of the ventilatory insufficiency in the 2 patients with tetralogy of Fallot (Cases 3 and 4, Table I) is not known. Neither had cardiac failure or pulmonary hypertension before operation. Both had a marked decrease in cardiac output after operation from unknown causes: 1, No. 3, had potassium asystole during bypass; the other did not. Experimental studies of pulmonary function following cardiopulmonary bypass by Schramel, Creech, and associates[8] have shown a decreased pulmonary diffusion capacity for several days after operation. The cause at present is unknown.

Indications for Use of Respirator.—Dyspnea, progressing to physical exhaustion and coma in some patients, was the clinical indication for the use of a respirator in the 3 patients with mitral valve disease (Cases 5, 6, and 7) and the 3 patients with pulmonary disease (Cases 8, 9, and 10). Severe hypotension and metabolic acidosis, not responding to blood transfusions and vasopressors, were the indications for the respirator in 2 patients (Cases 1 and 2) Moderate dyspnea was also present A respirator was used for the 2 patients with tetralogy of Fallot (Cases 3 and 4) because of a combination of dyspnea, arterial oxygen unsaturation, and low cardiac output

The respirator was used only after other simpler measures had failed These measures included high humidity, endotracheal suction to remove secretions, bronchodilators, sometimes aminophylline and hydrocortisone Cardiac failure was treated with digitalis, diuretics, and fluid restriction, and measurement and regulation of blood volume Attempts to manage the patients with tracheotomy alone were used in most instances, and the respirator begun only when this was unsatisfactory Our hesitation to use the respirator is evident from the fact that some of the patients were drowsy or comatose, hypotensive and sweating, with ineffectual respiration, when the respirator was started Although improvement may be dramatic under such circumstances, the respirator probably should have been used earlier

Results—Nine of the 10 patients made a satisfactory recovery The respiratory insufficiency was so severe in all of these patients that survival without the use of the respirator was considered unlikely The origin of the fatal pneumonia in Case 4 is unknown Aseptic precautions were routinely carefully observed in the management of patients on the respirator These included washing of the hands before tracheal aspiration and the use of sterile catheters Serious respiratory infection did not develop in any of the 61 patients treated with a respirator by Bjork and Engstrom[3]

The favorable outcome in 6 of the 7 patients with cardiac disease in this series was due to the fact that the respiratory insufficiency was due to reversible causes We have unsuccessfully used the respirator in a few other patients following cardiopulmonary bypass who were seriously ill with hypotension and coma in whom respiratory insufficiency was not a prominent feature Although respiratory function was sustained in these patients, circulatory failure and coma persisted and ended fatally

Our present concept of the value of the respirator is to support the patient during a period of transient decrease in respiratory function If the respiratory insufficiency is secondary to circulatory failure that does not improve, the respirator will not be of value Patients who may most frequently benefit from the respirator following operation are patients with pulmonary hypertension, often found with ventricular septal defect, and patients with mitral or aortic valvular disease with chronic cardiac failure before operation

SUMMARY

Ten patients with severe respiratory insufficiency were treated with a Morch piston respirator from 1 to 42 days Nine of the 10 patients recovered

The respiratory insufficiency resulted from chest wall trauma in 1 patient, followed pulmonary surgery in 2 patients, and followed cardiac surgery with cardiopulmonary bypass in 7 patients. In these 7 patients the cause of respiratory insufficiency was often uncertain. Chronic congestive failure and pulmonary hypertension before operation were the most likely causes in some of the group, but in others the cause was unknown.

A respirator has not been frequently used for respiratory insufficiency resulting from cardiac disease. The experiences presented here suggest that postoperative respiratory insufficiency following cardiac surgery may be successfully treated in some patients with a respirator until recovery of respiratory function occurs.

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(There was no discussion of this paper.)

THE INTRATHORACIC COMPLICATIONS OF SUBPHRENIC ABSCESS

David P. Boyd, M.D., Boston, Mass.

Over 100 patients with subdiaphragmatic space infection have been treated at the Lahey Clinic during the past 10 years. An interesting group of problems has resulted, due to a large surgical service, which included complex and secondary operations on the biliary tract, pancreas, stomach and spleen. A previous article[2] dealt with some changing concepts relative to the anatomy and pathology of the subphrenic spaces. These concepts will be briefly reviewed before the complications of this disease are considered here.

THE ANATOMY OF THE SUBPHRENIC SPACES

The time-honored anatomic and pathologic concepts of Barnard[1] have been widely accepted[3, 4] and are to be found in standard textbooks of surgery. From the anatomic standpoint it is commonly believed that the coronary ligament divides the superior surface of the liver into anterior and posterior compartments. Thus, anterior and posterior spaces are described on both sides and the nomenclature becomes cumbersome and confusing. The basis for this confusion is the fact that spaces are described which do not exist.

Fig. 1 shows how this misconception regarding the position of the coronary ligament causes confusion. The important consideration is that the coronary ligament suspends the liver not from above, as shown in this drawing, but from the dorsal aspect of the abdominal wall.

Fig. 2 shows the anatomic relationships of the suprahepatic area as we understand them. Thus, on the right side there are only two spaces—one above the liver and one below. The space which is usually designated "right posterior superior" does not exist. This can be readily confirmed at laparotomy or in the dissecting room. Since the right posterior superior subphrenic space is considered the most common site of infection, the importance of this point of confusion is apparent.

Fig. 3, a cross-sectional drawing, shows how the misapprehension may be further propagated. In this drawing, the coronary ligament and the bare area are shown in a superior position, thus giving rise to the appearance of an anterior and posterior space on the right and left sides. Study in the anatomy laboratory shows that no such space exists on either side.

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Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

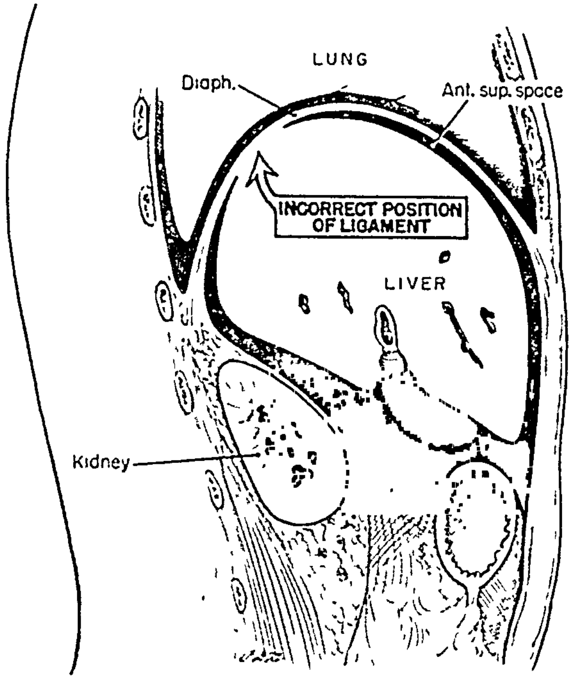

Fig. 1.—*For legend see opposite page.*

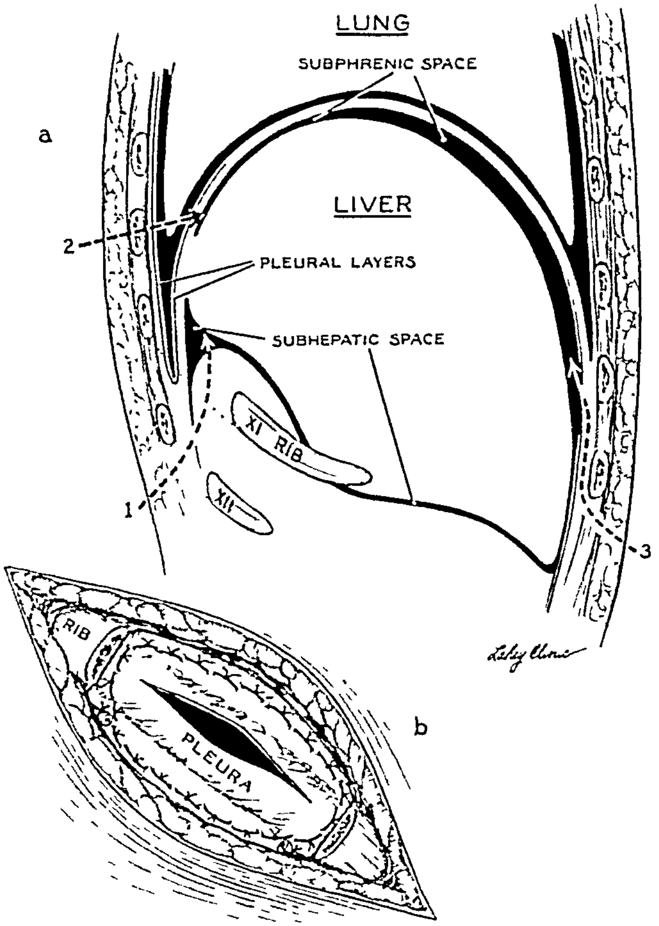

Fig. 2.—*For legend see opposite page.*

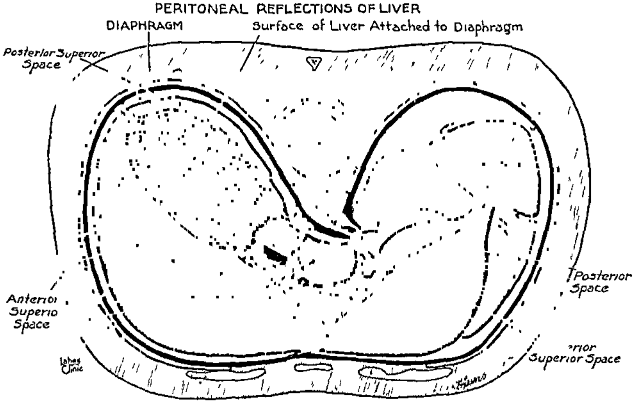

Fig. 3.—Usual type of drawing suggesting the presence anatomically of anterior and posterior spaces on both sides The spaces indicated above and designated "posterior superior space" on the right and "posterior space" on the left do not exist. Actually, the bare area and both triangular ligaments are considerably more posterior than the diagram suggests

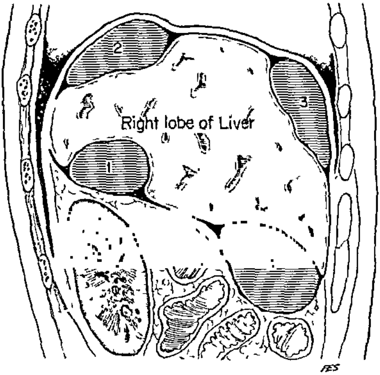

Fig 4.—*1*, Right posterior subhepatic abscess This site may be readily drained extrapleurally and extraperitoneally below or through the bed of the resected twelfth rib (Ochsner; Fig. 2 *1*). This type of collection is often termed "right posterior subphrenic" in standard texts.

2, Right posterior subphrenic abscess It is obvious now, when the anatomic relations of the coronary ligament are carefully drawn, that this abscess is considerably above the pleural reflection Therefore, it can be drained only by some modification of the Trendelenburg approach.

3, Right anterior subphrenic abscess The approach to this part of the subdiaphragmatic space is a subcostal incision on the right going extraperitoneally and extrapleurally (Ochsner).

4, Typical right anterior subhepatic abscess easily reached through the existing right rectus or subcostal incision

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Fig. 1—The right triangular ligament is usually depicted as dividing the superior surface of the liver into anterior and posterior spaces This error is sometimes even more exaggerated than shown above The proper anatomic relationships are shown in Fig. 2.

Fig 2—The very large areas occupied by the subphrenic and subhepatic spaces on the right side are shown *a*, The various approaches to these spaces are indicated: *1*, twelfth rib extraserous route (Ochsner); *2*, Trendelenburg transpleural route. The technique of su- the pleura to the diaphragm is shown in insert *b*

PATHOLOGIC ANATOMY

From the clinical and pathologic standpoint, the above remarks regarding anatomy represent an oversimplification. The normal anatomy should be clearly understood before pathology is considered, however. The presence of loculations in the subphrenic and subhepatic areas makes it essential that the site of infection be localized more precisely.

It has been emphasized that the subphrenic and subhepatic spaces are large, particularly on the right side. Characteristically, these large spaces become subdivided about their mid-points by the formation of pyogenic membranes. We are therefore compelled to acknowledge the presence of anterior and posterior subphrenic and anterior and posterior subhepatic abscesses. Fig. 4 shows typical collections.

COMPLICATIONS

The complications of subphrenic space infection are chiefly intrathoracic, since the septic process frequently spreads through the diaphragm into the pleural cavity or into the lung. Purulent exudate has a tendency to try to escape, and the soft diaphragm and lung constitute a less formidable barrier than do the rigid liver and posterior parietal structures. In 1 case, however, purulent exudate from an anterior subphrenic abscess on the right side perforated into the general abdominal cavity with diffuse peritonitis and rapid fatality.

The intrathoracic complications of subdiaphragmatic abscess will be discussed briefly under three headings: (1) serous effusion, (2) purulent subphrenic infection with perforation into the thorax, and (3) obstruction of the biliary tract with subdiaphragmatic biliary abscess and intrathoracic communication.

Serous Effusion.—

We have been interested in the nature and characteristics of the serous effusion which so frequently accompanies subdiaphragmatic abscess. We have learned that it is usually ipsilateral, but not always. It is seldom massive in amount unless cardiac disease is also present. It may be in evidence with subhepatic infection, but this is unusual. In most instances it indicates infection above the liver.

In a few instances, we have had the opportunity to study this fluid and have found that it is clear, pale yellow, and has a high neutrophil and protein content. It has always been sterile on culture. We were not able to determine any particular point of onset of this fluid in the course of subdiaphragmatic infection. It has not proved to be a therapeutic problem in any way.

Subphrenic Infection With Intrathoracic Communication.—

If the pleural cavity is free, perforation of purulent exudate into the chest produces empyema. This may be massive and result in very rapid toxicity; thus, unless prompt drainage of both thorax and subphrenic area is provided, death may ensue. In our experience, when prompt drainage of both spaces has been carried out, the lung has rapidly re-expanded and healing has occurred.

In the cases in which pleural symphysis is present, however, a fistula forms between the subphrenic area and the bronchial tree. This condition may follow one of two general forms. An acute fulminating type of necrotizing bronchopneumonia may occur, with rapid toxicity and death, or the course may be extremely indolent. The following case reports illustrate these categories.

A 42-year-old man was admitted to the hospital in June, 1944, with the diagnosis of carcinoma of the pancreas. This diagnosis was not substantiated at laparotomy, and the abdomen was closed. Convalescence was smooth and the patient was discharged 2 weeks following operation. Two years later, in July, 1956, he was readmitted. He had been in the hospital at his home town for a week or two with unexplained fever and, on the day before admission to the Lahey Clinic, had experienced a sudden episode of copious expectoration with rapid development of dyspnea and toxicity.

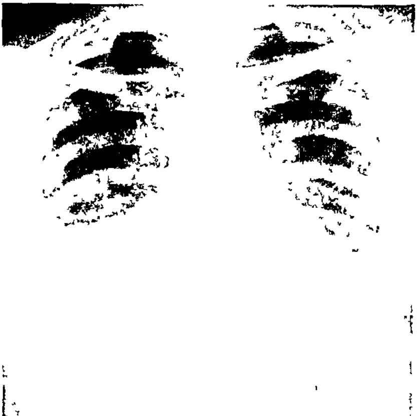

Fig 5—Marked elevation of right leaf of diaphragm in a patient with perforation of a subphrenic abscess into the bronchial system

The clinical picture and the x-ray studies (Fig. 5) suggested subdiaphragmatic abscess on the right side with perforation into the right lung and bronchial tree. Drainage of the subphrenic space was carried out, followed by tracheostomy. The patient improved for a few hours but became increasingly ill and died.

A number of these patients have survived, but this case is cited because of the fact that a postmortem examination was obtained. This revealed chronic pancreatitis without any evidence of purulent exudate anywhere except in the right suprahepatic space. This space had been adequately drained.

This case also illustrates the chronicity which is possible in subphrenic abscess. A purulent collection had presumably been present above the right lobe of the liver for 2 years without symptoms before perforation into the thorax occurred. It also demonstrates the severity of the resulting necrotizing bronchitis and bronchopneumonia.

Perforation into the chest may not be such a dramatic phenomenon in some cases, however, and may be almost of the occult variety.

An 18-year-old boy was seen at the clinic following perforation of an ileostomy with a catheter. The stoma was revised, and an attempt made to rinse out the abdominal cavity as well as possible.

A few months later, this boy was admitted with fever and leukocytosis. He stated that he had failed to gain weight. Roentgenographic examination was strongly suggestive of right subphrenic abscess (Fig. 6). This abscess was found and drained. During convalescence, Lipiodol was instilled into the sinus above the right lobe of the liver in order to determine its size, and filling of the bronchial tree resulted (Fig. 7).

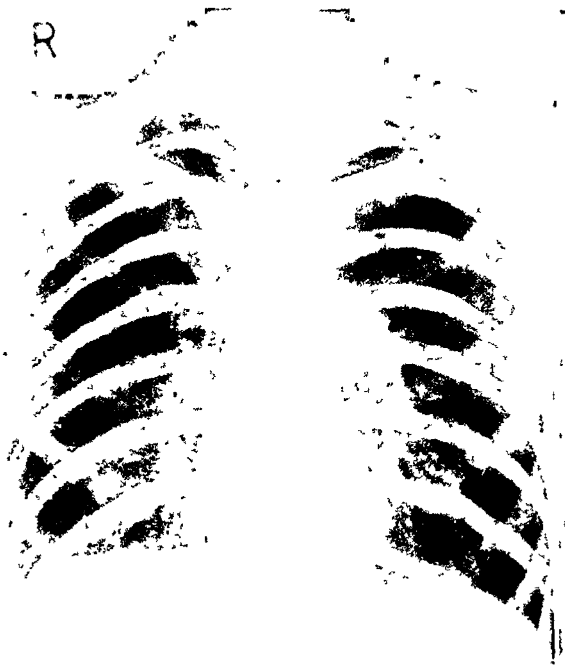

Fig. 6.

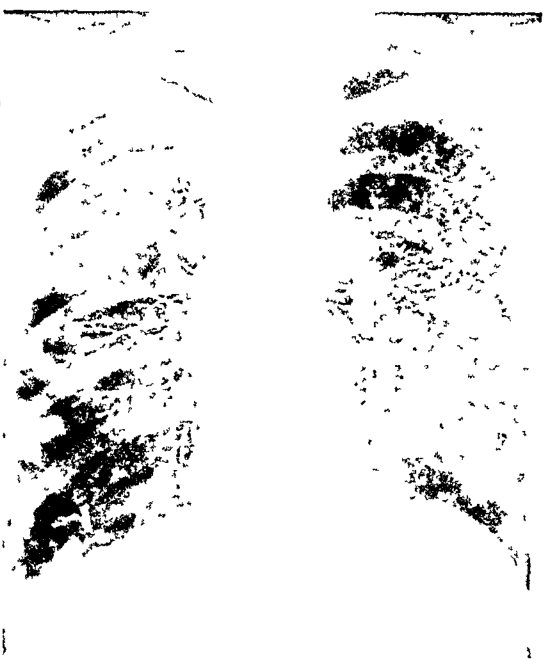

Fig. 7.

Fig. 6.—High fixed diaphragm with air fluid levels on right, indicating subphrenic abscess.

Fig. 7.—Instillation of dye into subphrenic space with filling of bronchial tree, indicating perforation of a subphrenic abscess into the lung.

Experience has shown that when drainage of the subphrenic area is carried out, the pulmonary lesion will usually heal. In most cases, lobectomy will not be necessary.

Biliary Communications With the Intrathoracic Cavity.—

In the course of our work with postoperative strictures of the bile ducts, we have encountered a number of patients in whom, following secondary or complex operations, subdiaphragmatic collections of bile have developed. These collections in turn have, at times, perforated into the thorax. Again, two sets of circumstances are possible. If the pleura is free, a large collection of bile accumulates in the intrathoracic cavity. This disturbs the intrathoracic dynamics and may cause tension unless evacuated promptly. Furthermore, secondary infection is almost sure to ensue. Management of these patients consists of correcting the intrathoracic dynamics by trocar drainage, followed by proper attention to the obstructing lesion in the biliary tract.

At times, however pleural symphysis is present and when perforation occurs, it occurs into the bronchial tree, resulting in a bronchobiliary fistula. The type of pneumonitis and bronchitis which is found in this circumstance is a very serious one because of the necrotizing effect of bile. Prompt drainage of the subphrenic area is essential to stop this expectoration of bile. The lesion cannot be healed until the obstruction in the common duct has been removed, however.

GENERAL PRINCIPLES OF [illegible]MENT

S[illegible] these principles have been implied in the paragraphs above. One speci[illegible] relative to the site of drainage will be mentioned, however. The typ[illegible]s which we see today is commonly a right posterior subphrenic one [illegible]) It will be seen from the drawing that this abscess is best trea[illegible]athoracic, transpleural drainage. The abscess designated 1 in F[illegible] [illegible]urse, be drained extraserously. This is not truly a subphrenic a[illegible]wever, it is subhepatic. The type of abscess which we see following secondary operations on the upper abdominal viscera is different from the type of abscess which characteristically followed generalized peritonitis in former years.

SUMMARY AND CONCLUSIONS

In this brief presentation I have attempted to make three major points. (1) The anatomy of the diaphragm and the suprahepatic area can be made simple [illegible] (2) Subphrenic abscess as we see it today is a more chronic and ind[illegible]ent a[illegible] than it has been in the past. Thus, it may be more dangerous fro[illegible] the st[illegible]point of intrathoracic complications (3) For cure of subdiaphragmatic a[illegible] as we now see it, a transpleural approach is required.

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DI[illegible]SSION

DR [illegible]RENCE H RUBEN[illegible] [illegible]ago. Ill—I enjoyed the excellent [illegible] by Dr. I[illegible] and I merely rise to [illegible] [illegible]t he has said; namely [illegible] pulmonar[illegible] [illegible]lications one must first [illegible]

I have had experience with 3 patients who presented themselves with pulmonary problems. The outstanding symptom in each case was hemoptysis associated with mucopurulent sputum.

[Slide] The first case was a man who presented himself with suspected carcinoma of the lung with hemoptysis, mucopurulent sputum, weight loss, cachexia, and an opacity in the right lower lobe. An interesting finding on bronchoscopy was that the anterior medial basal segment was hyperemic and the pus seemed to be coming from that area.

In going back into his history, he had had previous biliary disease; jaundice the year before. At exploratory operation, he was found to have an absence of the gall bladder. On careful examination we found a slightly tender anterior bulge of the right lower chest. This turned out to be the subphrenic abscess, which was drained, and the patient made a complete recovery.

This roentgenogram is an anterior posteroanterior projection of the same patient showing the suspect right lower lobe involvement.

Another case was that of a woman who also presented herself with a primary picture of pulmonary disease, expectoration of pus, and blood. Again on bronchoscopy it was noted in this particular case that the anterior medial basal segment of the right lower lobe was also involved with hyperemia and pus coming from this area.

A history of gall bladder disease was elicited. A subphrenic abscess was suspected, discovered, and drained. The patient made a good recovery.

The next case—I am sorry I don't have a slide to show—was a most interesting case, because the patient was admitted as an emergency due to massive exsanguinating hemoptysis. An anterior biliary fistulous drainage tract in the epigastrium was closed. The etiology of the fistula was never thoroughly established. Subsequent to fistula closure, the patient coughed bile and developed massive hemoptysis which required a lingulectomy because the fistulous tract extended from the left lobe of the liver to the lingula. This was demonstrated by bronchogram preoperatively. A life-saving lingulectomy was done.

Subsequently, the patient has had an abdominal exploration. No true cause for the biliary fistula could be established. The origin of the fistula was from the anterior portion of the left lobe of the liver. A jejunobiliary anastomosis was made and the patient made a good recovery.

The pulmonary disease subsided only after the underlying subphrenic pathology was adequately treated.

DR. DUANE CARR, Memphis, Tenn.—I wish to thank Dr. Boyd for bringing a very important subject to our attention, and I would like particularly for the younger men to note how carefully Dr. Boyd sutured the pleura to the diaphragm *before* he crossed the pleural space. Of course it is impossible to suture it if one is going to put a trocar, needle, or what-not across the pleural space in searching for an abscess which he may be unfortunate enough to find by needle, thereby contaminating the pleural space very thoroughly. For that reason some of us who have dealt with these abscesses over a number of years hesitate to probe for them with needles.

What Dr. Boyd has said, with which I agree completely, applies to the pyogenic or pyrogenic infections, I think without exception. I would like to ask him what his attitude may be toward a surgical approach to the pure amebic subphrenic infections, including liver abscesses. In our experience we have not done nearly so well with these by a surgical approach as we have with the pyogenic organisms.

DR. ADRIAN LAMBERT, New York, N. Y.—I recently had occasion to summarize the cases of subphrenic abscesses at Roosevelt Hospital between 1940 and 1957. In this group of 29 patients on whom 33 procedures were done, the relevant fact is that 93 per cent of these patients presented themselves with pulmonary complications, including an elevated diaphragm in 78 per cent, atelectasis in 63 per cent, pain and pleurisy in 56 per cent, and the presence of chest fluid in 50 per cent.

The second point that I think is of interest is that in these patients the interval of time between the development of the subphrenic abscess and the time that they were drained was twice as long in those who had antibiotics as in those who didn't, showing that the antibiotics will mask the symptoms of subphrenic abscess; and the usual pain, splinting of the abdomen and so forth are not present when you have the patient under antibiotic therapy.

Two empyemas developed in this group, and we felt that they developed secondary to traumatic thoracentesis where the needle had been introduced into the abdomen through the pleural space, so that caution should be taken in aspirating the pleural fluid, so that the subphrenic collection is not drained traumatically through this aspiration

DR. BOYD (Closing).—In answer to the first discusser, I perhaps should have made the point that the biliary type of complication is much more serious from the standpoint of lung destruction. In our experience it has also been necessary to do a lobectomy for lung disease after bronchobiliary fistula. This has not been the case after the ordinary type of subphrenic infection with bronchial fistula

If there were time one would like to have paid tribute to former Presidents of this Association and the present one, who have contributed much to our knowledge of subphrenic disease

In answer to Dr. Carr, I might say that this group which we have treated, although quite large, is in a sense a selected series Very few of these patients with subphrenic abscess have developed this complication following generalized peritonitis In other words, they have been mostly of our own doing, that is, these abscesses have followed upper abdominal surgery which we have done ourselves. This may be the reason why there have been so many subphrenic rather than posterior subhepatic abscesses. In this series, Dr. Carr, we have not encountered any amebic abscesses, so that I am unable to answer your question

THE EARLY ELECTIVE SURGICAL APPROACH TO THE TREATMENT OF TRAUMATIC HEMOTHORAX

Morris M. Culiner, M.D. (by invitation), Benson B. Roe, M.D., and Orville F. Grimes, M.D., San Francisco, Calif.

THE PRESENCE of blood in the pleural cavity represents a potential hazard and may prove to be a difficult problem to manage. The severity of the condition and its management depend upon several factors: the volume of blood and its rate of accumulation, the possibility of contamination, and the tendency of blood to undergo loculation and organization. The success of conservative management of hemothorax depends upon the absorptive capacity of the pelura and the ability to evacuate the pleural space by means of a needle or thoracostomy tube. Repeated futile attempts at treatment by conservative means, however, may only delay more definitive forms of therapy and increase their difficulties. The time required to absorb blood from the pleural space may serve to defeat conservatism in the management of hemothorax. If the blood becomes clotted, the possibility of evacuating blood through a tube or needle is lost and decortication becomes necessary to free the encapsulated lung. Frequently a more aggressive approach to the treatment of traumatic hemothorax not only answers the unknowns in the problem but permits them to be brought under control and materially reduces the over-all morbidity and duration of treatment.

Decortication of the lung is a well-accepted procedure in the treatment of clotted hemothorax. Most observers recommend that 4 to 6 weeks should elapse before elective decortication is attempted. This implies that the conservative approach to the evacuation of blood from the pleural space has failed. In civilian practice, when delays in evaluation can be kept at a minimum, the failure of conservative treatment should be recognized within several days. In these instances the thorax can and should be evacuated completely by early elective thoracotomy.

In order to assess our experience in the management of traumatic hemothorax and to justify early elective surgical intervention in certain patients, 43 case histories were reviewed. Most of these patients were cared for at the San Francisco General Hospital. This study extends over a period of 7 years, 1951

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to 1958. Of the 43 patients, 27 were treated with needle aspiration or tube drainage, 10 with early thoracotomy, 4 with delayed decortication, and 3 with rib resection for empyema. The following selected case histories illustrate some of the problems which occurred in the management of these patients.

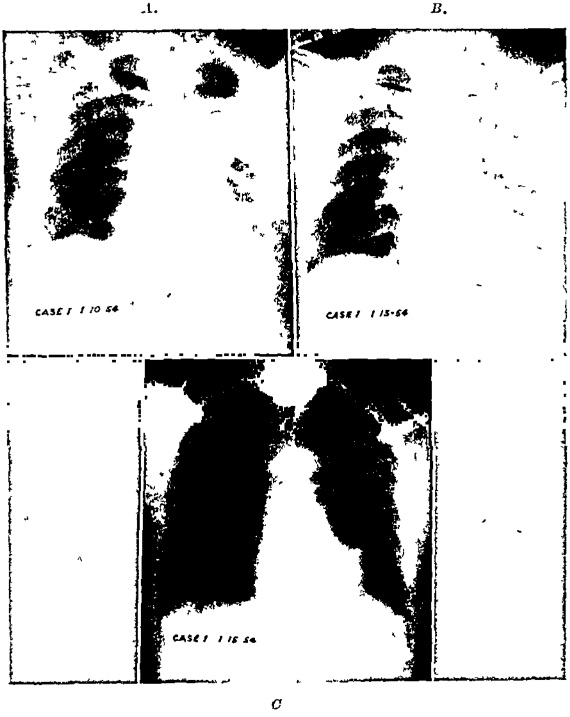

Fig. 1.—Case 1. *A*, The roentgenogram taken on admission shows haziness of the left hemithorax, due to hemopneumothorax.

B, The roentgenogram shows partial clearing following aspiration of 1,300 ml. of blood by the tubal thoracostomy and thoracenteses.

C, This film taken 5 days after trauma demonstrates a satisfactorily clear pleural space.

CASE REPORTS

Case 1.—A 36 year old Negro man sustained a stab wound from a penknife in the second left anterior intercostal space on Jan. 10, 1954. He was admitted to the hospital shortly after injury. A portable supine roentgenogram showed opacification of the left hemithorax (Fig. 1, *A*). Thoracentesis yielded 1,000 ml. of air. Tube thoracostomy was established 6 hours after the injury and suction was applied to the tube. Fifteen hundred milliliters of bloody fluid was evacuated (Fig. 1, *B*). Two transfusions of whole blood were administered. The thoracostomy tube was removed on the following day since it no longer functioned properly. During the next 4 days, needle thoracenteses were performed and a total of 300 ml. of bloody fluid was removed. A roentgenogram obtained on Jan. 15, 1954, 5 days after injury, showed the left hemithorax to be clear and lung expansion to be complete.

Comment: This case history illustrates the well-accepted concept that prompt tube thoracostomy serves to evacuate blood satisfactorily from the pleural space in most instances. The majority of the patients in this series were successfully managed by conservative means.

CASE 2.—A 38-year-old Negro man was stabbed in the third anterior right intercostal space and was admitted to the hospital within 30 minutes of injury. Although needle thoracentesis yielded 1,700 ml. of bloody fluid, evacuation of the pleural space was incomplete.

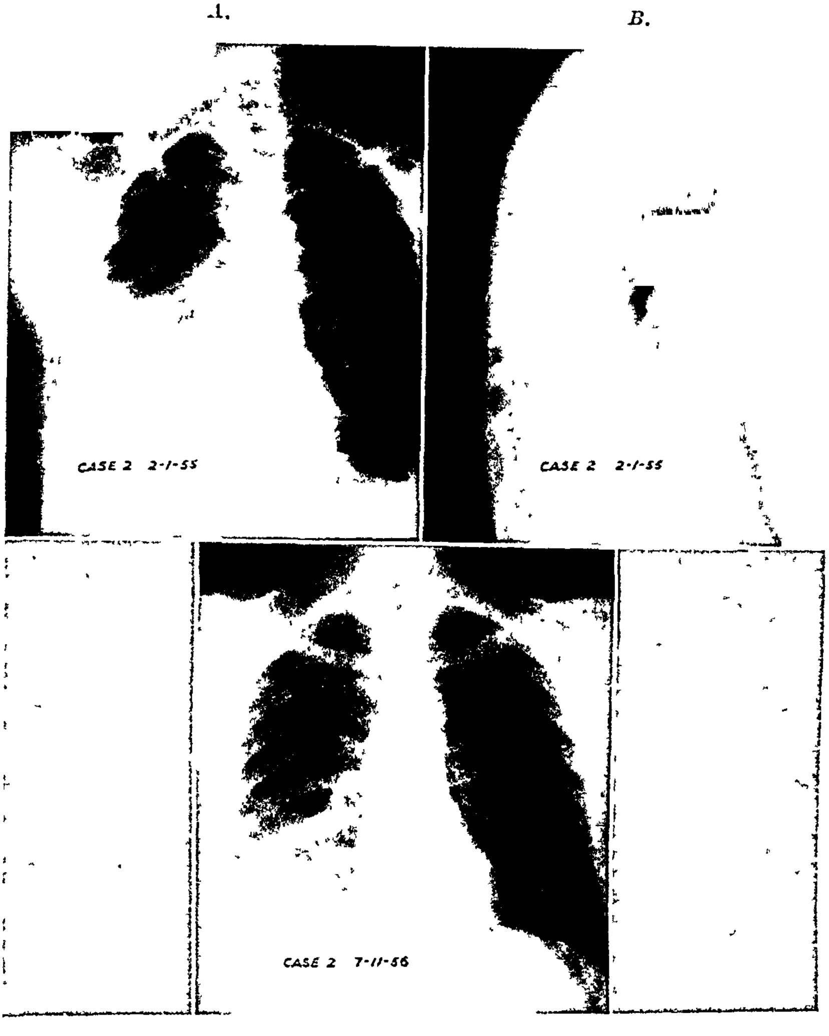

Fig. 2.—Case 2. *A* and *B*, Anteroposterior and lateral films taken 8 days after injury show a clotted hemothorax despite repeated early thoracenteses.

C, This roentgenogram demonstrates residual fibrotic organization of the hemothorax, 18 months after injury. Note the elevated and adherent right diaphragm.

A thoracostomy tube was inserted shortly after admission and was attached to 15 cm. of water suction. In spite of this therapy a considerable volume of blood remained intrapleurally. Thoracenteses were performed repeatedly in an attempt to obtain more complete evacuation of the pleural cavity. Very little bloody fluid could be aspirated by needle. Roentgenograms obtained on Feb. 1, 1955, 8 days following trauma, showed a large amount of blood loculated posteriorly in the right hemithorax (Fig. 2, *A* and *B*). At this time the patient signed out against medical advice. On July 11, 1956, 18 months after the stab wound was incurred, the patient was re-admitted to the hospital for treatment of a different disease. A posteroanterior roentgenogram of the chest obtained at that time (Fig. 2, *C*) showed relatively good lung re-expansion. However, blunting and elevation of the diaphragm at the base of the right chest were present.

Comment. Although needle thoracenteses and tube thoracostomy on the day of injury resulted in evacuation of 1,700 ml. of bloody fluid, a large pocket of loculated blood clot still remained in the pleural space. After the tube was removed no effective treatment was possible. This patient spontaneously resorbed and organized most of the residual blood during the next 18 months but was left with a basal fibrothorax.

It is impossible to state whether a significant degree of respiratory reserve was lost in this patient since no specific studies were obtained. However, fluoroscopic observations of other patients with similar radiologic findings of blunting and elevation of the costophrenic angle have demonstrated markedly restricted ipsilateral diaphragmatic excursions. The clinical effects of this varied and depended upon other factors, such as the presence of parenchymal disease and the basic physiologic requirements of the patient's occupation.

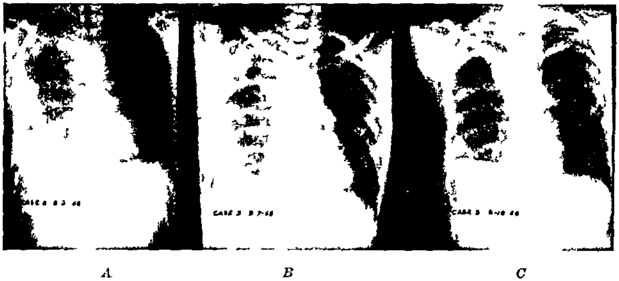

Fig. 3.—Case 3. *A*, Postoperative roentgenograms show hemopneumothorax with collapse of the right lung and the contracted hemithorax.
B and *C*, Roentgenograms taken [illegible] days and 13 days after decortication show that the right lung has re-expanded and the right hemithorax is quite clear.

CASE 3.—A 14-year-old Negro boy underwent exploratory thoracotomy to determine the nature of a right paramediastinal mass. Biopsy of the nodal mediastinal mass at that time revealed a tuberculous granuloma. Postoperatively the lung remained partially collapsed (Fig. 3, *A*). The patient was transferred to the San Francisco General Hospital on Aug. 21, 1956, 12 days after exploration. On admission to the hospital, examination showed markedly restricted respiratory excursions on the right. Pulmonary function studies indicated a moderate decrease in pulmonary reserve.

Roentgenograms and the aspiration of bloody fluid demonstrated a post-thoracotomy hemopneumothorax with partial collapse of the right lung. A thoracostomy tube was inserted into the pleural space on Aug. 24, 1956, and negative-pressure suction of 150 cm. of water was applied. Only 400 ml. of bloody fluid were evacuated during the next 30-hour period. Roentgenograms before and after tube thoracostomy revealed that no significant re-expansion of the lung had resulted. Decortication was believed to be advisable. On Sept. 5, 1956 (4 weeks after the initial traumatic hemopneumothorax) decortication was carried out. The patient did well postoperatively (Fig. 3, *B* and *C*). Intermittent positive pressure was administered frequently. Breathing exercises were administered and the patient showed a striking objective increase in respiratory function. The ultimate lung expansion was excellent and later respiratory function studies indicated a marked increase in reserve.

Comment: In this case, hemopneumothorax of 2 weeks' duration was first treated by tube thoracostomy and high suction. This treatment proved to be ineffectual in obtaining re-expansion of the lung and evacuation of pleural blood. Decortication was carried out 4 weeks after the initial hemopneumothorax. Decortication produced a good functional result.

Case 4.—A 31-year-old Negro man was stabbed in the right upper anterior part of the chest on June 8, 1956. He was in shock when admitted to the hospital but his condition was stabilized by the administration of whole blood and plasma. He coughed up blood at this time, which suggested that the lung had been penetrated. A thoracostomy tube was inserted immediately and suction was applied (Fig. 4, *A*). Only 500 ml. of blood was aspirated through the thoracostomy tube during the next 2 days. Roentgenograms taken 4 days after the initial trauma showed that a massive hemothorax was still present (Fig. 4, *B*). The patient was in good condition and showed no evidence of continued intrathoracic bleeding.

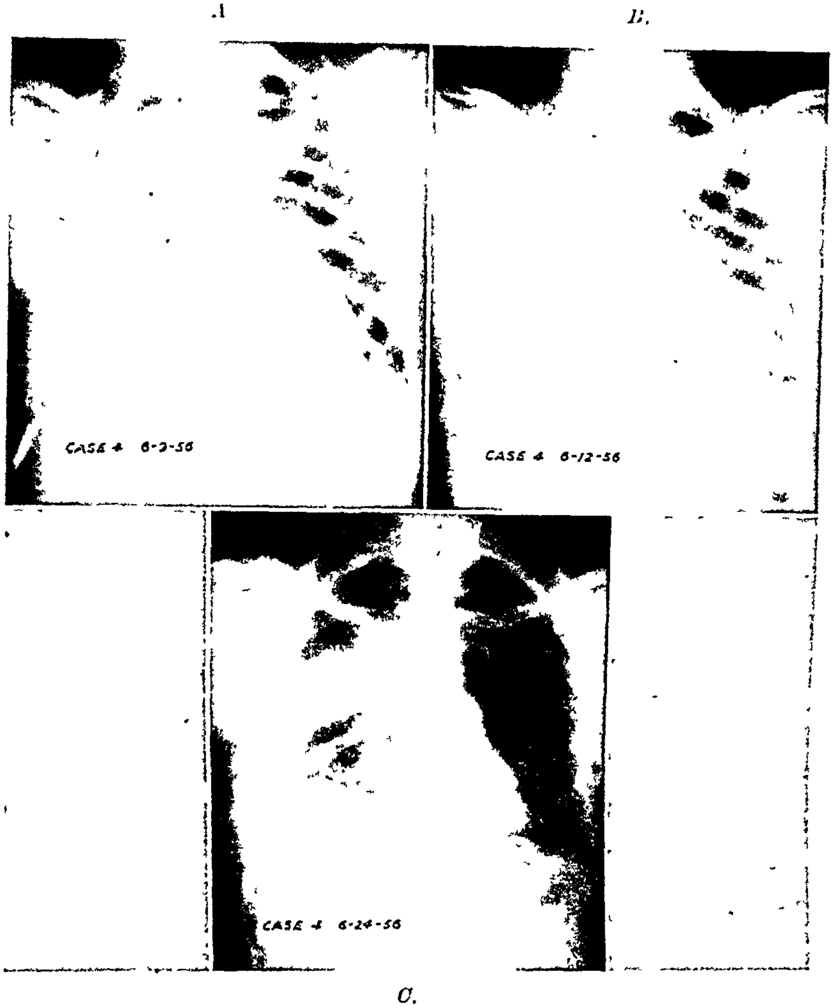

Fig. 4.—Case 4. *A*, A roentgenogram taken 1 day after injury shows the thoracotomy tube in the pleural space which is filled with clotted blood.

B, The residual hemothorax on the fourth day following injury is evident.

C, This film taken 12 days after early elective thoracotomy demonstrates the parenchymal hematoma and relatively clear pleural space.

On the fourth day after injury an elective thoracotomy was performed. Approximately 1,500 ml. of clotted blood was removed. The pulmonary parenchyma had been lacerated by the stab wound but re-expansion of the lung was immediate and complete. No technical difficulty was encountered in the removal of the blood clot Films taken on the first post operative day and on the twelfth postoperative day showed excellent lung expansion. The area of injury to the lung appeared as a hematoma in the mid lung field (Fig. 4, *C*). The patient's further postoperative course was uneventful.

Comment: Conservative management was attempted unsuccessfully. The failure of tube thoracostomy was recognized early. At this point therapy might have been directed along two other courses than that elected. On the one hand, the catheter might have been removed and the ability of the pleura to absorb the fluid then relied upon. On the other hand, a deliberate waiting period of 4 to 6 weeks could have preceded decortication. In each of these two choices the risk of failure and of complications must be recognized. Beyond that, such therapy prolongs hospitalization. After early elective thoracotomy this patient was home on the twenty-fourth day after injury.

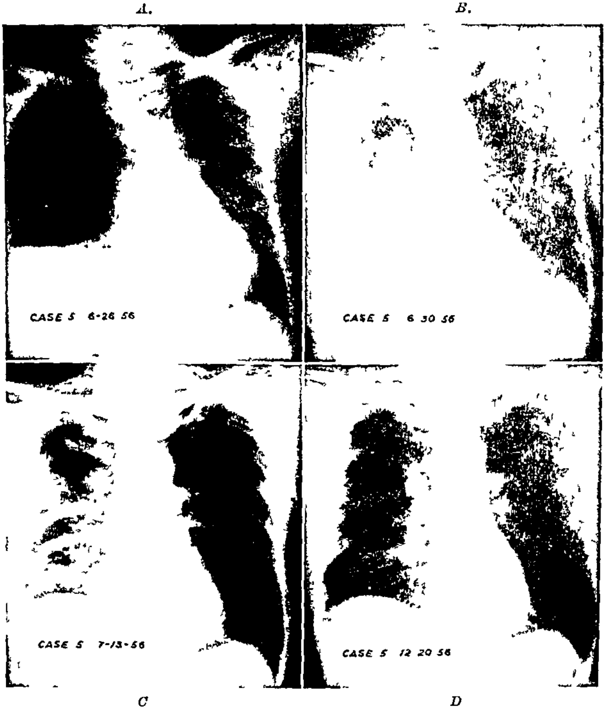

Fig 5.—Case 5 *A*, This film taken on the day of admission shows massive spontaneous hemopneumothorax resulting in mediastinal displacement to the contralateral side

B, Tubal thoracostomy produced an incomplete evacuation of the blood Marked residual pulmonary collapse is shown

C, A film taken 10 days following early elective thoracotomy for clotted hemothorax shows a relatively clear pleural space

D, The follow-up roentgenogram demonstrates excellent lung expansion 5 months following thoracotomy

CASE 5.—A 59-year-old Chinese man was admitted to the San Francisco General Hospital on June 26, 1956, with a history of tightness of the chest and shortness of breath for the previous 4 days. There was no history of injury. The initial roentgenogram showed an extensive right hemopneumothorax with mediastinal shift to the left and adhesions at the right apex (Fig. 5, *A*). The apical adhesions suggested that spontaneous rupture of the lung had occurred at this site.

Needle thoracentesis on the day of entry yielded 2,000 ml. of bloody fluid and 700 ml. of air. A follow-up roentgenographic study showed incomplete evacuation of the hemopneumothorax. Consequently on June 28, 1956, tube thoracostomy was performed but this also failed to evacuate the hemothorax although all air was removed and improved lung expansion followed. The tube was removed on June 30, the fourth hospital day, because its use had not resulted in adequate improvement. Elective thoracotomy was performed on July 3, 1956, 7 days after admission and approximately 11 days after the onset of hemopneumothorax. Thirteen hundred milliliters of fluid and clotted blood was removed. Satisfactory re-expansion of the lung was immediately obtained. An apical adhesion to which clotted blood had become adherent appeared to be the source of bleeding as postulated preoperatively. The operation was not technically difficult. The patient was discharged on the seventeenth hospital day, 21 days after onset of the hemopneumothorax. Roentgenograms at this time showed good lung expansion (Fig. 5, *C*). Roentgenographic studies 5 months later showed an excellent result (Fig. 5, *D*).

Comment: This patient with hemopneumothorax was initially treated conservatively with tube thoracostomy. When this therapy proved ineffective, elective thoracotomy was carried out on the seventh hospital day. On the seventeeth hospital day, 10 days postoperatively, the patient was discharged with a totally satisfactory result.

CASE 6.—A 31-year-old white man was stabbed in the fourth left intercostal space on Aug. 4, 1956. Needle thoracentesis was performed shortly after arrival at the hospital and within a few hours following injury. Since adequate improvement was not obtained a thoracostomy tube was inserted and suction was applied. Despite the early insertion of the tube into the pocket of pleural blood, as demonstrated on the roentgenograms (Fig. 6, *A* and *B*), only 400 ml. of bloody fluid was aspirated. Most of the blood had clotted and remained intrapleurally. The patient's condition stabilized within 12 hours after injury and after 2 units of whole blood had been administered.

Tube drainage with suction yielded only 200 ml. of blood during the next 18 hours. Repeated roentgenograms again showed a large left posteroinferior density of the hemithorax. Fifty-six hours after injury, an elective thoracotomy was performed. Approximately 1,300 ml. of blood, clot, and fluid was removed without difficulty. The lower lobe of the left lung was found to be completely compressed by the blood and clot but it re-expanded readily. The patient was discharged with excellent lung aeration on Aug. 19, 1956, the fifteenth day after injury (Fig. 6, *C* and *D*).

Comment: Although this patient was treated for hemothorax by tube thoracostomy within several hours of injury, the hemithorax was inadequately evacuated by this method. Elective thoracotomy with evacuation of the clotted blood was carried out 56 hours after injury. The functional results were excellent and the degree and duration of illness and disability were minimized, in addition to eliminating the possible complications of infection of a clotted hemothorax.

CASE 7.—A 40-year-old white woman was admitted to the hospital on Nov. 18, 1955, a few minutes after being in an automobile accident. Roentgenograms of the chest showed fractures of the eighth, ninth, and tenth ribs on the right side (Fig. 7, *A*). These initial films showed no other abnormalities and specifically did not reveal evidence of fluid in the right pleural space. Follow-up roentgenographic studies 3 days after the injury showed a large amount of fluid within the right pleural space (Fig. 7, *B*). Thoracentesis yielded 800 ml. of bloody serous fluid. Subsequently 2,000 ml. of serosanguineous fluid formed but satisfactory expansion of the lung was obtained by simple needle evacuation (Fig. 7, *C* and *D*).

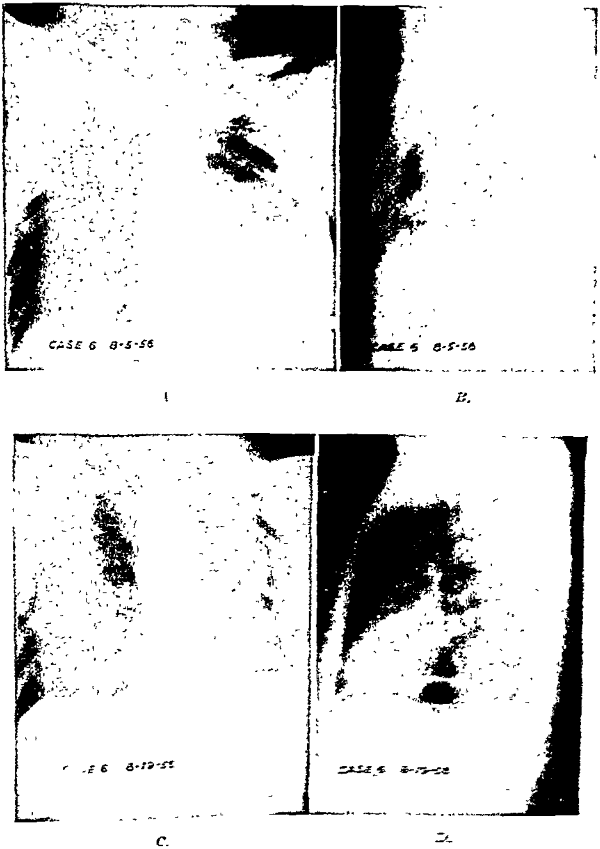

Fig. 6.—Ca[illegible] hemothorax. On [illegible] thorax. *A* and *B*. The [illegible] lateral view [illegible]

C and *D*. T[illegible] early elective th[illegible] roentgenograms [illegible] may show [illegible]

Comment: [illegible] case is of [illegible] of accumulation [illegible] fluid or blood [illegible] initially clear p[illegible]ral space [illegible] the necessity of [illegible]ow-up films and [illegible] radiologic findin[illegible]

CASE 8.—A 25-year-old Negro man was stabbed through the left fourth interspace anteriorly on Oct. 23, 1958, and was admitted to the hospital within 1 hour following injury. At that time he was dyspneic and had a pulse rate of 120. Respirations were 30 per minute and blood pressure was 100/80 mm. Hg.

A roentgenogram of the chest revealed a left hemopneumothorax (*Fig. 8, A*). Two intercostal catheters were inserted and connected to continuous suction. During the next 6 hours, 2,700 ml. of bloody fluid was evacuated from the left pleural space and 2,500 ml. of whole blood was administered intravenously. The thoracostomy tubes continued to drain about 300 ml. of blood per hour. Eight hours after injury, a thoracotomy was done. At operation, 1,000 ml. of blood clot and 800 ml. of bloody fluid were removed from the left pleural space. The only active bleeding was from the intercostal muscles around the stab wound. A short laceration of the lung was present but was not bleeding at the time of thoracotomy.

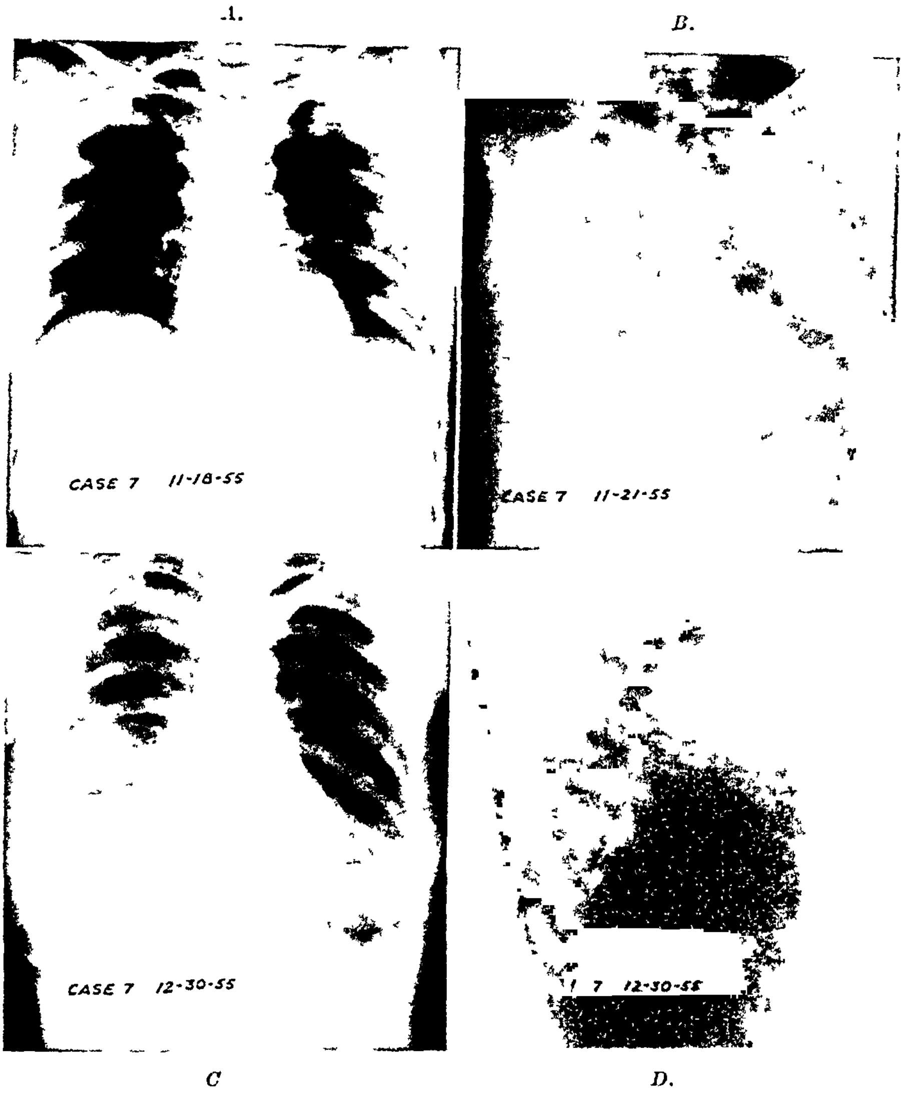

Fig. 7.—Case 7. *A*, A clear right hemithorax is seen shortly after injury.
B, A delayed accumulation of serosanguineous fluid is demonstrated 3 days after injury.
C and *D*, Thoracenteses resulted in a clear hemithorax following delayed hemothorax formation.

All bleeding was controlled with suture ligatures. Expansion of the lung was readily obtained and maintained (Fig. 8, *B*). Pleural fluid was demonstrated radiologically on the sixth postoperative day. Thoracentesis yielded 1,200 ml. of blood tinged serous fluid and the hemothorax was completely cleared by this (Fig. 8, *C*). The patient's postoperative course was otherwise uneventful and he was discharged on the tenth postoperative day.

Comment: This patient demonstrated continued and significant bleeding after early tube thoracostomy and evacuation of 2,700 ml. of blood were carried out. Thoracotomy was thought to be necessary and was performed 8 hours after the patient was admitted to the hospital. At thoracotomy there was 1,900 ml. of blood and clot within the pleural space despite the presence of 2 tubes to which suction had been constantly applied.

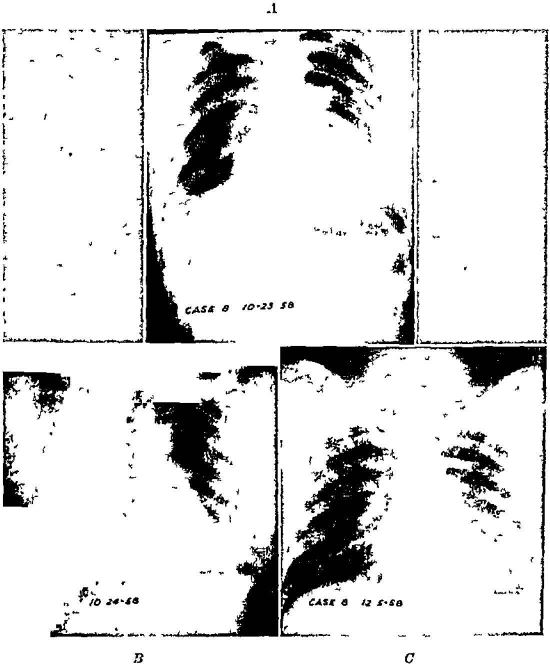

Fig 8—Case 8 *A, The roentgenogram demonstrates the post-traumatic hemopneumothorax.*

B, This film was taken 1 day following trauma and thoracotomy A total of 1,500 ml of blood and clot had been evacuated by tube and thoracotomy

C, The follow-up roentgenogram shows satisfactory clearing

DISCUSSION

The care of patients with early traumatic hemothorax cannot be rigidly standardized. A basic plan of treatment can be formulated and this can be appropriately altered as new developments ar[illegible] The results of [illegible] therapy will necessarily influence the subsequent s[illegible] [illegible]ement. [illegible] hemothorax the hemorrhage usually cea condition becomes stable with fluid and blood replacement. In these patients thoracotomy is not necessary as a lifesaving measure. The problems of paramount importance are the preservation of maximum pulmonary function and the prevention of sepsis. Whether a significant decrease in pulmonary reserve occurs as a result of hemothorax depends upon the volume of clotted blood compressing the lung, the development of infection, and the production of a fibrous restriction of the respiratory movements. The resulting respiratory embarrassment also depends on the pre-existing pulmonary reserve.

The more complete the evacuation of blood from the pleural space the better is the functional result. The earlier the blood is removed the more complete is the evacuation, since later clotting and loculation will prevent emptying of the pleural space by conservative means.

In many patients with traumatic hemothorax of minor degree, intrapleural blood can be aspirated by needle within the first few hours following trauma. Needle thoracentesis carries only a minimal risk of pleural contamination unless it is repeated often. This technique also carries very little danger of pneumothorax due to puncture of the lung. Certain disadvantages, however, must be kept in mind; the small caliber of the needle does not permit rapid removal of blood; the needle easily becomes plugged and complete removal of blood from the pleural space is not often accomplished in this manner.

Should the amount of blood in the pleural cavity be at all significant, that is, sufficient to obscure the diaphragmatic leaf and costophrenic angle, tube thoracostomy should be used as soon as possible. The method of Betts and Lees[1] may be helpful. With this technique, the trocar used for insertion of the intercostal catheter remains briefly in place. The catheter is moved around all areas of the pleural space while constant suction is applied to it. After all possible blood has been evacuated, the trocar is removed. The catheter remains intrapleurally and is attached to suction to evacuate blood which remains and serous fluid which may continue to ooze into the pleural space.

Often, although the pleural cavity may have been cleared initially, re-accumulation of fluid may be noted after several days. This fluid may result from continued bleeding or from the exudative reaction of the pleural surfaces, not only to the initial trauma, but also to the blood which remains. When early roentgenograms show the pleural space to be devoid of fluid or if complete evacuation of the hemothorax has been carried out, follow-up roentgenograms should be obtained several days later to demonstrate whether re-accumulation has occurred.

The clotting of blood in the pleural cavity may occur within a few minutes or may be delayed for several days following injury. Often, despite the early use of needle thoracentesis and tube thoracostomy, large amounts of blood may remain clotted in the pleural space. Our experience with the use of proteolytic enzymatic agents has been disappointing. Use of these agents has frequently produced an increased volume of fluid which can be aspirated from the pleural space. It is quite likely that the increased fluid resulted largely from the exudative reaction of the pleural surfaces to the irritating agents.

The significant problem is the selection of patients in whom removal of clotted pleural blood by open thoracotomy is warranted. A review of the cases of several patients with hemothorax who were essentially untreated has indicated that resorption or fibrotic organization of blood and concomitant re-expansion of the lung may occur spontaneously. Lung re-expansion as indicated by roentgenograms may occur in the presence of a restrictive fibrotic pleural process which can significantly inhibit respiratory excursions. For this reason a state of lung expansion in itself does not indicate good ventilatory function. In problems such as these, pulmonary function studies, especially bronchospirometry, may provide the only objective determination of the decrease in pulmonary function produced by the fibrotic pleural process. Without similar studies recorded prior to injury even these studies have only limited significance.

The decision for surgical evacuation of blood must be based on a clinical assessment of the following factors: (1) the ventilatory excursions of the thoracic wall, and (2) roentgenographic demonstration by posteroanterior and lateral views of the pleural blood and its position. This assessment can be made as accurately within a few days as after 4 to 6 weeks. During this period, minimal resorption of clotted hemothorax occurs. During the same period, however, there can be resolution of pleural reaction and clearing of the roentgenogram. However, the radiologic picture of clotted hemothorax must be differentiated from that of pleural reaction and thickening. These conditions may resemble each other on posteroanterior roentgenograms. Lateral views, however, generally distinguish between the 2 entities since a clotted hemothorax frequently shows a posteroanterior triangular opacified area due to loculation. A diffuse circumferential opacification suggests pleural reaction. This differential point was emphasized by Tuttle.

When it becomes apparent that conservative means of removing blood from the pleural cavity are inadequate and that optimum functional results require the evacuation of clotted blood, operation is carried out without delay. Early elective thoracotomy for decompression of the lung and evacuation of blood clot has been performed within periods ranging from a few hours to 17 days following the formation of hemothorax. These operations have been performed with no great technical difficulty and full lung re-expansion has been obtained as readily as when decortication has been employed 4 to 6 weeks after trauma.

Some patients show evidence of continuing severe intrapleural bleeding after initial evacuation of a hemothorax. These patients should be treated by early elective thoracotomy to control the source of bleeding and to evacuate the pleural space completely.

By performing a thoracotomy within a few hours or days after injury one can control the hemorrhage, evacuate all blood clots, permit and maintain immediate lung re-expansion and, in most instances, prevent the development of empyema. With adequate replacement of whole blood these patients are managed satisfactorily during operation. The source of bleeding is most frequently a lacerated intercostal vessel. In those cases where early elective thoracotomy has been utilized, lung re-expansion has been easily obtained and the postoperative course has been quite uncomplicated. By immediate or early lung expansion with obliteration of the dead intrapleural space and removal of the excellent culture medium, empyema has been prevented in all cases. The economic factors of early operation and convalescence are quite important to the patient. No benefit is derived from a delay of 4 to 6 weeks from the time of onset of clotted hemothorax to the time of evacuation.

In this series of 43 patients treatment was as follows: (1) 27 patients were treated by needle thoracentesis with or without tube thoracostomy, (2) 10 patients were treated by early elective thoracotomy within a few hours or days following trauma, (3) 4 patients were treated by delayed decortication 4 to 6 weeks after injury, and (4) 2 patients were untreated until empyema occurred and then were treated by rib resection.

Of the 27 patients treated by needle thoracentesis with or without tube thoracostomy, 26 did well. One patient treated early in the series developed empyema. This patient had been ineffectively managed by repeated thoracenteses and instillation of antibiotics and proteolytic agents. Early thoracotomy with evacuation of blood clot would have been much more appropriate therapy in this case.

Of the 10 patients treated by early elective thoracotomy for hemothorax, 9 patients recovered promptly. The one death in the series occurred 12 hours after secondary thoracotomy for hemothorax. The primary sternum-splitting thoracotomy had been done to remove an anterior mediastinal neurilemmoma. A secondary thoracotomy was carried out 48 hours after the primary procedure. The cause of death was not definitely established. It was probable, however, that there was undue delay in carrying out the secondary thoracotomy to control the postoperative hemothorax.

The 4 patients treated by delayed decortication, at intervals of 4 to 6 weeks following trauma, had uneventful postoperative courses and satisfactory results. All of these patients came under our treatment at a late stage. The average period of hospitalization for the patients who underwent decortication was 48 days. In contrast with this, the average stay of patients treated by early elective thoracotomy was 19 days.

Three patients whose condition was complicated by infection were treated by rib resection and drainage.

In 1 patient, empyema developed immediately in a hemothorax after he had suffered a gunshot wound. The first sample of blood aspirated from the pleural space revealed the infecting organism. The second patient signed himself out of the hospital after several days only to return in 2 weeks with frank empyema. The empyema spaces in these patients were sufficiently small so that decortication was not believed to be warranted. The third patient developed a hemothorax following resection for coarctation. The hemothorax was treated by thoracenteses only, and the patient developed empyema 18 days afer the primary procedure. This patient should have had early elective thoracotomy rather than repeated ineffective thoracenteses. As a result of the ill-advised therapy with aspiration and instillation of antibiotics and proteolytic agents, he was hospitalized for 2 months All 3 of these patients were treated by rib resection and open drainage Ultimately re expansion of their lungs was satisfactory and the empyema cavities eventually healed

SUMMARY

Selected case reports from a series of 43 patients with hemothorax are presented to demonstrate the problem and results associated with the various forms of treatment A rationale is developed for selected early surgical intervention as the treatment of choice when conservative measures are unsatisfactory Experience has indicated that the morbidity and mortality of thoracotomy are low and that the results are definitive and complete in removing the hemothorax The hospitalization and disability periods are significantly shortened Early elective thoracotomy is recommended for clotted hemothorax *in preference to a deliberate delay for cortex formation*

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DISCUSSION

DR CHARLES T READ, Phoenix, Ariz —I hesitate to get up before this group again to discuss streptokinase, but I didn't hear the word mentioned in the paper that was just delivered I heard proteolytic enzyme mentioned one time I hope it was not one of the competitive drugs

I am sorry that I happened to be the man who came to this meeting, but just happened to have no slides with me But I venture to say that in my own experience with post resection problems, which I have shown before this group, they look much worse than some of these cases that were shown, and I feel that enough emphasis has not been placed upon this particular maneuver If the authors did not use this procedure, I think they have passed up a good portion of the armamentarium offered in taking care of these patients' problems, because with the use of closed thoracotomy one has the advantage of using enzymes quite frequently until the chest is evacuated, and in many instances very good results can be obtained

If these gentlemen have used this, I would like to hear more about it. If they haven't, I would like to remind them of the work that has been carried on previously.

DR. JOSEPH A. WEINBERG, Long Beach, Calif.—I interpret this paper, which I certainly enjoyed, as advocating an earlier recognition of the patient who will need more than simple, watchful treatment, aspiration, or possible tube thoracotomy.

I would like to point out that the pleural surfaces have remarkable absorptive power for clearing the blood from the hemothorax, and that I trust that the remarks that have been made here will not be interpreted as advocating open thoracotomy with evacuation of blood and clots in all patients. I am sure that the authors do not mean that, since more than half of their patients were treated by more conservative means. Operations are not without danger and there should be clear indications for their use.

I also would advocate conservatism in the waiting period while it is being determined whether or not the patient will need an open thoracotomy with evacuation of clot and possible decortication. Frequent aspirations may be the very thing that makes open operation necessary at a later time because of the introduction of contaminating bacteria with subsequent infection.

DR. ROBERT K. BROWN, Denver, Colo.—I agree 100 per cent with the authors when they say that these things should be cleaned out and normal physiology restored. I thought Dr. Weinberg would make the point I want to make, but he didn't. I think it is very important in the thoracotomy for this situation to do it through an intercostal incision and leave an intact 12 rib hemithorax for the best and most efficient possible restoration of ventilatory function after operation.

DR. JAMES V. MALONEY, JR., Los Angeles, Calif.—Two years ago we published our own results in a group of 40 cases of traumatic hemothorax with very similar results. We interpreted our experience as indicating that surgical decortication should be used less often and later, rather than more often and earlier.

There has been a general trend toward the surgical treatment of clotted hemothorax since the very fine and classic work of Dr. Samson. We became worried, however, that this trend was being carried too far. In self evaluation I returned to Baltimore, where I had treated a large number of these patients over a period of 8 or 9 years. I was able to find follow up chest films (taken for incidental diseases, tuberculosis surveys, et cetera) in 40 cases. Thirty of the hemothoraces were due to gunshot and stab wounds and ten were due to operation. We were amazed to find that on the incidental chest films taken from 3 months to 7 years later there was not a single instance of clotted hemothorax in which there was any detectable evidence of chest abnormality (with the exception of retained missiles) in any of the 30 cases due to stab wounds or gunshot wounds. Postoperative hemothorax was a more difficult problem and required surgical decortication in 3 cases and enzymatic decortication in 5. Empyema was encountered with enzyme therapy and, like Dr. Culiner, we had one death in the operative group.

The technical ease of decortication and the restoration of the chest film to normal give this operation a special appeal to the esthetic sense of the surgeon. But the major question is whether or not the operation is necessary. I am sure there is merit to both the conservative treatment that we recommend, and also to the idea that Dr. Culiner has presented today. I don't know which point of view is correct, but it is appropriate that the subject be brought up and re-evaluated so that we can obtain a definitive answer to the problem in the next several years.

DR. EDOUARD D. GAGNON, Montreal, Quebec.—We, too, have been interested in early thoracotomy when indicated in hemothorax. I would like to refer specifically to 3 such cases where there was traumatic hemopneumothorax because, in these cases, without thoracotomy (the two first ones on the day of injury and the third one 5 days after injury, when first seen by us) there might have been very severe or dire consequences, because the source of hemorrhage was a "split" lung.

The most interesting thing to me was that in the first case the right upper lobe had been split wide open by this closed injury to the chest, as if with a meat cleaver, and the bleeding was coming from the lobar veins, whereas the air was leaking out of multiple bronchioles plus an additional tear to the lobar bronchus. This patient was treated by lobectomy.

In the second case, the left upper lobe and left lower lobe were split open as if with a knife on their posterior aspect, the same pathology was present in the third case, but on the right side. When the lung was fitted back into the posterior gutter it seemed to me, in these 3 cases that the injury had been produced by the anterior forward edge of the vertebral column and the lobes had been split open as if they had been cut with a knife, or with a meat cleaver.

The second case required resection because the lung was very damaged. In the third case we were able to suture the sliced parenchyma and the patient made an uneventful recovery.

It is, I think, worth remembering such possibilities in closed injuries to the chest. If the trauma has been severe enough to split the lung and occasion hemorrhage, early thoracotomy or earlier thoracotomy, in these cases might save a few lives.

Maybe the reason we surgeons have not recognized this condition more often is that a great majority of these cases probably end up in the civic morgues.

DR PAUL C SAMSON, Lafayette, Calif.—This paper by Drs Culmer, Roe and Grimes has interested me very much, and I am sure they will not be too hard on me if I disagree with them somewhat.

I think no one will argue for a moment that there are cases in which early thoracotomy in traumatic hemothorax is a very wise procedure. They indicated the fact, as did Dr Gagn [illegible] cases of continued bleeding thoracotomy is certainly necessary.

On the other hand, in the cases under discussion, and I would like to limit my remarks to those patients in whom we wish to preserve lung function, I doubt very much if 25 per cent of the time we need to do a thoracotomy to achieve the result desired. You will note that the essayists operated on 25 per cent of their patients.

Their series is small, and I presume that this is their entire experience, at least since they started doing thoracotomy, but I would like to remind them that we have cared for [illegible] thoraces for a number of years. Perhaps blood clots more frequently in San Francisco than it does in Oakland, but as we have reviewed briefly our series of cases at the County Hospital, where we see 20 to 30 traumatic hemothoraces a year, I cannot find evidence of [illegible] operated in more than 1 out of 12 or 15 cases. In other words, it is not the fact that [illegible]ver operate on hemothoraces, but we don't operate as much as is done in San Francisco.

I hope it doesn't date me if I remind you that even today thoracotomy carries at least a [illegible]tical risk, and that we should not operate any more than is absolutely necessary.

My only advice in closing is that I think they should use the needle more and the scalpel less.

DR LAURENCE MISCALL, New York, N Y.—I would like to enthusiastically support Dr Samson.

During [illegible] last war when the late Dr Elliot Cutler was being inducted into the Royal College of S[illegible] he asked me to look over some of the data from the hospitals which were not thorac[illegible] I reviewed 200 consecutive cases of hemothorax which were treated initially in [illegible]her than thoracic centers where supposedly decortication and other definitive c[illegible]re to be done. I found that when repeated aspiration or tube drainage w[illegible]racic exercise as indicated in the field, evacuation and station hospitals a[illegible]f these 200 patients recovered completely and never had to undergo any [illegible]rax.

I think [illegible] of importance. I do not believe that one can transp[illegible] all the war ex[illegible] Many of our military patients had to come to thoracic centers for secondary operation for hemothorax because of other factors. Many had retained large foreign bodies often with infection. Clotted or infected hemothoraces requiring drainage or decortication were therefore more common than might be expected in civil practice.

I would like to make one more observation since I noted that tubes were placed in some chests quite early. Frequently have I seen a too enthusiastic assistant resident treat a stab wound of the chest by immediate tube drainage and to his utter surprise found out in a short time that he is sucking out from the patient more blood than he can easily replace.

DR. JOSEPH GORDON, Albuquerque, N. Mex.—Now that Dr. Samson has opened the wound, I thought that I would like to add just a little bit of salt into it by bringing these factors to your attention. Commonly, when an injury to the chest occurs and hemothorax is present, there are two other factors; that is, most often there is contusion of the lung, in addition to which the body defense mechanism puts the diaphragm and the chest at rest. The diaphragm elevates itself to a "mean position" in the respiratory phase, and the rib cage resists movement to protect itself from pain caused by the injury.

Now, to swing this treatment over a little bit more to the more conservative side, one of the features that we should recognize, and Dr. Weinberg indicated that the pleurae have a large absorptive ability, is that it is necessary to return this body to a physiologic function as quickly as possible. If you don't have to put a needle in the chest because of respiratory distress it is best to exercise these patients. Make the patients move their chests, make them move their diaphragms; they will more rapidly return to physiologic function and heal the injury which has occurred while absorbing the fluid.

DR. JOSEPH L. LUCIDO, St. Louis, Mo.—We have had an experience with 300 traumatic chest injuries at the St. Louis County Hospital in St. Louis, Missouri, during the past 10 years. We have followed the points emphasized by Doctors Tom Burford, Paul Samson and associates in their papers published after the Second World War.

You will recall that approximately 15 per cent of all the hemothoraces which they reported became clotted and 85 per cent remained liquid early in the course of the disease. We have, therefore, used two, three or even four large water-seal tubes early in the course of the disease of these patients. If maximum expansion and evacuation has not been obtained in 72 hours we have then resorted to massive use of Tryptar or Varidase, and I am mentioning the names. We have used Tryptar or Varidase massively 7 or more days before resorting to thoracotomy.

If the above has not been successful we have then, as stated, resorted to thoracotomy and decortication. Exploratory thoracotomy has been used during the first 48 hours in individuals with massive uncontrollable hemorrhage, or other severe associated injuries of an emergent nature. I recall that last year we reported 25 instances in which we explored individuals who had ruptured diaphragms.

Our thoracotomy percentage has been less than 5 per cent in the individuals whom we have treated in this manner.

DR. CULINER (Closing).—I realized that bringing up this subject was somewhat like bringing coals to Newcastle, and I thought it might precipitate a little bit of discussion, not this deluge.

I would like to indicate that we have heard of streptokinase, streptodornase, and Tryptar and have used them extensively earlier.

[Slide] We feel that certainly with the use of proteolytic agents one can always aspirate a great deal of fluid following their instillation, whether it is in 6 hours or 24 hours. My own feeling is that the fluid that one aspirates following their use is the fluid that one causes by their use.

This particular patient illustrates one whom we treated with these magic drugs, and this film of September 19 shows the hemothorax present in the right lower portion of the pleural space. On this day streptokinase and streptodornase were instilled, and on the following day we had this degree of pulmonary collapse and formation of jelly-like material, which we later evacuated by thoracotomy. Our own feeling is that with the use of streptokinase and streptodornase we have not been as successful as many of the papers on the subject would indicate, and therefore we use it less, probably, than other services.

We are also fully cognizant of the fact that the absorptive capacity of the pleural surfaces is quite marked. We haven't been as fortunate as Dr. Maloney in getting follow-up films. We have tried very hard to have patients treated in San Francisco County Hospital return for follow-up films. It has been difficult for us. In those few of whom we have been able to get follow up films, in patients who refused therapy and who had a significant degree of hemothorax initially, we have found that many of them showed quite a marked pleuritic reaction with elevation of the diaphragm. Fluoroscopic examination of these has revealed inhibited respiratory excursion of the diaphragm and the lower hemithorax.

Perhaps the fog in San Francisco clots the blood more readily than it does in Oakland. Our 27 cases handled in that manner were quite satisfactory to us, but in 10 cases we felt it necessary to do early elective thoracotomy.

THE SURGICAL TREATMENT OF PEPTIC ESOPHAGITIS

Frederick S. Cross, M.D., George V. Smith, Jr., M.D. (by invitation), and Earle B. Kay, M.D., Cleveland, Ohio

INTRODUCTION

What is presently referred to as peptic or reflux esophagitis was first described by Quinke in 1879[21] and by MacKenzie in 1884.[17] It has gradually evolved as a definite clinical entity through the work of numerous clinical investigators[1, 4, 5] whose observations have been substantiated by laboratory experimentation.[3, 14]

When peptic esophagitis becomes so severe as to result in intractable pain, bleeding, stenosis, or perforation, medical therapy must be abandoned and some form of surgical therapy considered. As to what constitutes proper surgical treatment for these devastating complications of esophagitis has been a stimulus to surgical investigators for a number of years. A variety of procedures have been offered, ranging from phrenic nerve paralysis,[20] gastric resection,[18] esophagogastrectomy,[24] and hiatal hernia repair,[11, 16] to rather complicated plastic procedures on the esophagogastric junction.[2, 12, 22]

It is difficult to draw categorical conclusions as to the efficacy of any given procedure from reviewing the literature since, in many instances, conclusions are based on an experience obtained from the analysis of relatively few patients. In a recent study of 66 patients with reflux esophagitis, seven different operative procedures, or combinations thereof, were performed on 60 patients.[23] No single combination was done more than seven times. In another similar series of 60 patients with reflux esophagitis, there were no fewer than eight types of operations done.[11] The largest experience was with a combination of gastric resection and hiatal hernia repair performed on 14 patients.

Perhaps part of the confusion as to proper therapy, medical as well as surgical, but more particularly surgical, lies in the fact that everyone may not be talking about the same thing when he refers to esophagitis. Moersch and his associates[19] have aptly stated that esophagitis is not a single disease entity, but rather a group of conditions of related origin. Esophagitis secondary to prolonged vomiting differs markedly from that resulting from the nighttime

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puddling of gastric secretion after passage through an incompetent hiatus. In addition, Barrett adds a third type occurring in an esophagus lined with columnar mucosa.

Further confusion as to the proper operation for reflux esophagitis results from the presence of conditions existing in combination with the esophagitis. For instance, a hiatal hernia is frequently present, there may be an associated gastric or duodenal ulcer, or the esophagitis might be the result of surgical destruction of the cardiac sphincter mechanism, as in esophagogastrectomy. There is no disagreement that the damaging effects of acid peptic juice on the vulnerable esophageal mucosa must be curtailed if esophagitis is to be cured, but how to weigh the significance of these contributing factors in the light of adequate therapy poses a problem, and leads to the variations in opinion existing today.

The purpose of the present report is to review critically a group of patients with reference to the degree of existing esophagitis and to the presence of contributing etiological factors, to re-emphasize the role of hiatal hernia in the production of peptic esophagitis, and to propose reconstruction of the cardiac sphincter mechanism, as in hiatal hernia repair, as the logical treatment of this disease.

DEFINITION OF TERMS

For reasons previously stated, it is extremely important to define terms as accurately as possible when discussing the treatment of reflux esophagitis. For the purposes of this study, esophagitis has been categorized primarily as that existing with a hiatal hernia, and that in which no demonstrable hiatal hernia was present. However, the fact that no hiatal hernia was demonstrated does not necessarily preclude the existence of one. The degree of esophagitis has been graded into severe, moderate, and minimal. It is somewhat difficult to categorize esophagitis in this manner with extreme accuracy, but, inasmuch as it is possible, this was done on the basis of x-ray and esophagoscopic findings as outlined in Table I. Any patient with significant bleeding, stenosis, or perforation of the esophagus was listed as having severe esophagitis. Dysphagia alone

TABLE I CLASSIFICATION OF REFLUX ESOPHAGITIS

TYPE	ESOPHAGOSCOPY	X RAY
Mild	Reddening and edema of mucosa Prominent longitudinal folds Hyperplastic mucosal changes Reflux of gastric juice	Reducible concentric hernia Peristaltic abnormalities Reflux of barium
Moderate	Linear erosions Spasm and edema Friable, easily bleeding mucosa Reflux of gastric juice	Reducible concentric hernia Reflux of barium Spasm or narrowing of terminal esophagus Peristaltic abnormalities Irregularity of mucous membrane of distal esophagus
Severe	Ulceration with bleeding *Granular denuded areas* Marked edema and spasm Stenosis Reflux of gastric juice	Irreducible concentric hernia *Shortening of terminal esophagus* Ulceration of mucous membrane Reflux of barium Stricture of terminal esophagus

was not considered a symptom suggesting stenosis, since dysphagia can result from associated neuromuscular changes in the esophagus as well as from stenosis.[9] In most instances, the hernia was of the concentric or direct type in which the acute angle of entry of the esophagus into the stomach is lost. If the hernia was irreducible, with associated narrowing or shortening of the esophagus, the patient was placed in the severe category (Fig. 1); whereas, patients with reducible hernias, for the most part, were placed in the moderate or minimal categories (Fig. 2). Patients with erosions or ulcerations determined by esophagoscopy were not necessarily placed in the severe category unless there was evidence of esophageal narrowing or shortening in addition. Esophagoscopy was particularly useful in evaluating patients for placement in either the moderate or minimal categories. Frequently the mucous membrane changes seen in minimal esophagitis were minimal indeed. However, if they were associated with the visible regurgitation of gastric juice on esophagoscopy,

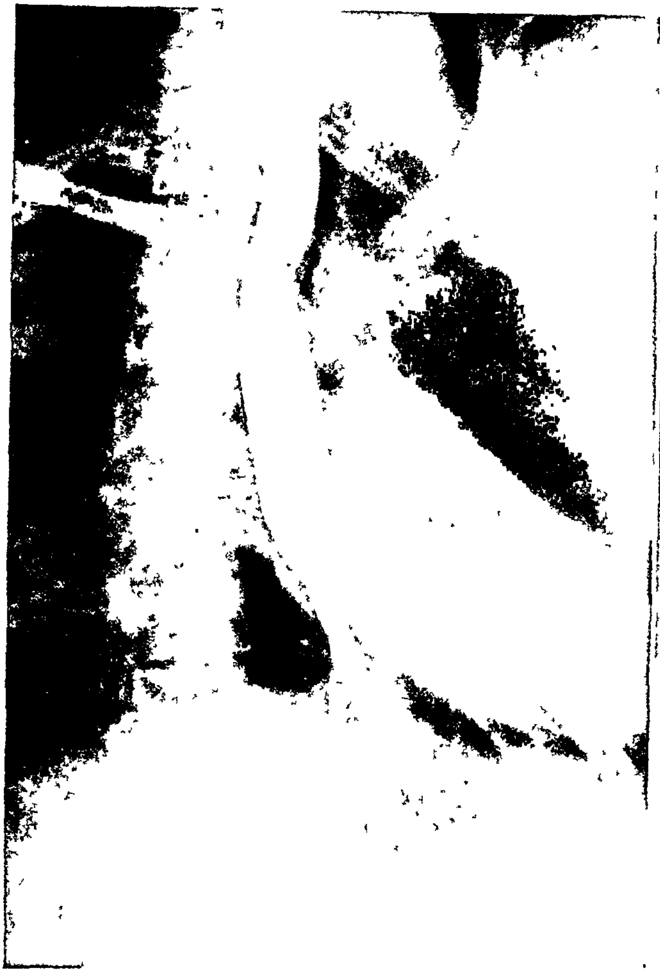

Fig. 1

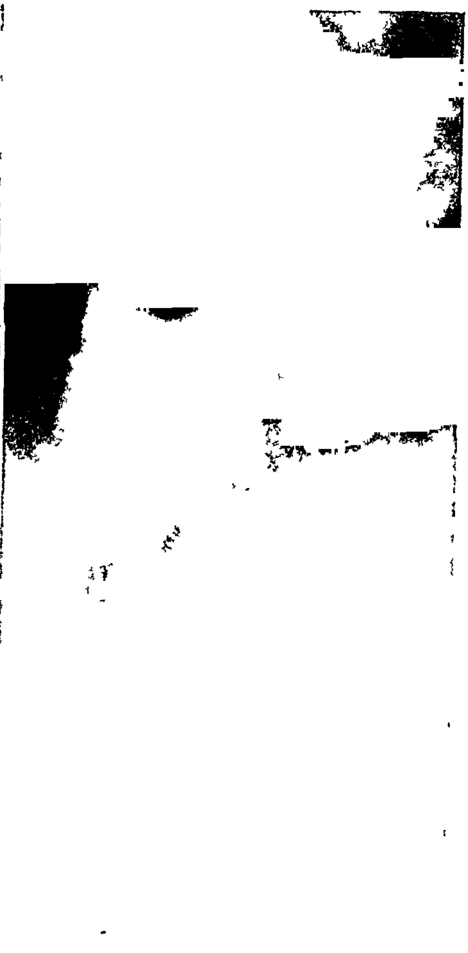

Fig. 2.

Fig. 1.—Severe esophagitis characterized by an irreducible hiatal hernia with stricture and shortening of the esophagus.

Fig. 2.—Typical x-ray appearance of a concentric, reducible hiatal hernia associated with minimal to moderate esophagitis.

or with some peristaltic abnormalities of the terminal esophagus on x-ray examination, the patients were retained in the study Since it has been noted that severe pain may exist in the presence of little demonstrable esophagitis, pain alone was not used as a guide in grading the degree of esophagitis present As a matter of fact, many patients with severe pain, but without good objective evidence of esophagitis, were eliminated from the study There were likewise discrepancies noted in the size of the hernia, the severity of symptoms present, and the degree of esophagitis demonstrated by esophagoscopy

Virtually all the cases of esophagitis were of a more or less chronic nature but admittedly a few were fairly acute, brought on by vomiting, or by dietary or alcoholic excess All the patients undergoing surgery had esophagitis of a chronic nature in terms of duration of symptoms, and most had been on a previous medical regimen

PRESENTATION OF MATERIAL

The present report represents the continuation of a study of 55 patients with esophagitis reported in 1956[8] From January, 1949, to Dec 31, 1958, 130 patients, ranging in age from 27 to 84 years, have been seen with varying degrees of esophagitis In 103 (79 per cent) of these patients, a hiatal hernia was present, and in 27 (21 per cent) patients no hiatal hernia could be demonstrated This distribution is in accord with the reports of other investigators

The symptoms in these individuals existed for varying periods of time and were the usual ones of substernal pain radiating through to the back, and heart burn and dyspepsia, usually made worse by food and alcohol indiscretion as well as by lying down Bleeding was frequently present, rarely as massive hemorrhage, more frequently occult in nature Dysphagia was not a constant finding The esophagograms of all the patients were reviewed to confirm the presence or absence of a hiatal hernia and to attempt to correlate the x-ray findings, symptoms, and the findings reported by esophagoscopy The majority of patients were subjected to esophagoscopy by us to ascertain the degree of esophagitis present All of the hiatal hernias were of the concentric type, with the exception of two classified as paraesophageal Two patients have been lost to adequate follow up examination, and 2 patients died postoperatively, leaving 126 patients in whom the results of treatment could be evaluated

Factors in the development of esophagitis other than a hiatal hernia were ascertained, and these are listed in Table II In 103 patients with esophagitis and hiatal hernia, the hiatal hernia was the only apparent cause for the esophagitis in 83, while 20 patients had other significant lesions as listed Fourteen patients had evidence of an associated gastric or duodenal ulcer, 1 of whom had had a previous cardioplasty One patient had had a previous gastric resection for duodenal ulcer, and another a gastroenterostomy In those individuals with esophagitis and no demonstrable hiatal hernia, no specific etiological factor could be found in 10, while the other 17 patients had a specific precipitating event or lesion associated with the development of the esophagitis (Table

TABLE II. ASSOCIATED LESIONS IN ESOPHAGITIS WITH HIATAL HERNIA

No associated lesion	83
Duodenal or gastric ulcer	9
Duodenal ulcer, vomiting	1
Duodenal ulcer, vomiting, gastric tube	2
Duodenal ulcer, cardioplasty	1
Gastric tube	1
Scleroderma	1
Cholecystitis and cholelithiasis	2
Varices, cirrhosis, duodenal ulcer	1
Gastric resection for duodenal ulcer	1
Previous gastroenterostomy	1
Total	103

III). Seven of these patients had evidence of a gastric or duodenal ulcer. Again, 1 patient in this group had had a previous gastric resection for a gastric ulcer.

TABLE III. ASSOCIATED LESIONS IN ESOPHAGITIS WITHOUT HIATAL HERNIA

No associated lesions	10
Gastric or duodenal ulcer	5
Vomiting	
Acute perforation	2
Acute ulcers with bleeding	2
Chronic esophagitis	1
Ulcer, vomiting, gastric tube	1
Cardioplasty	3
Cardioplasty and duodenal ulcer	1
Ectopic gastric mucosa	1
Previous gastrectomy for gastric ulcer	1
Total	27

TREATMENT

The treatment of peptic esophagitis may be medical or surgical. Surgical treatment is reserved for those patients developing the complications of intractable pain, significant bleeding, stenosis, and perforation. Medical treatment has been considered as definite therapy in those patients falling into the following categories: (1) acute esophagitis, such as produced by prolonged and severe vomiting, (2) certain individuals in whom the esophagitis is not associated with a hiatal hernia, and (3) esophagitis in those patients with hiatal hernia in whom elective surgery is contraindicated or refused.

Proper medical therapy has been well established and consists of a bland diet, antacids, elevation of the head of the bed and, if stenosis exists, esophageal dilations with a Jackson-Plummer dilator over a previously swallowed string.

The majority of patients with hiatal hernia received an adequate trial of medical therapy prior to surgery. Hiatal hernia repair was done essentially by the technique described by Allison[1] utilizing the transthoracic approach. In certain instances of short esophagus, transplantation of the esophageal hiatus to the dome of the diaphragm, with associated phrenic crush and extensive freeing of the proximal esophagus for added length, was necessary. The acute angle of entry of the esophagus into the stomach was assured in some of the patients by suturing the terminal esophagus to the adjacent gastric fundus, while, in others, the fundus of the stomach was simply sutured to the dome of the diaphragm. In no instances were associated drainage operations on the pylorus, gastric resections, or other ancillary procedures performed. Postoperatively, the patients were advanced rather rapidly to a regular diet, maintaining an ulcer regimen only if the symptoms of esophagitis persisted for that short interval of time during which the esophageal lesions were healing. Occasional postoperative dilations were necessary in those individuals with esophageal stricture.

RESULTS

The results of treatment in the 130 patients constituting the basis of this report are summarized in Tables IV and V. Only 2 patients in the entire series were lost to follow up study. There were 2 postoperative deaths, 1 following closure of a spontaneous perforation of the esophagus, the other following the repair of a hiatal hernia. Morbidity was that usually associated with

TABLE IV TREATMENT OF ESOPHAGITIS WITH HIATAL HERNIA

RESULTS	DEGREE	CONSERVATIVE TREATMENT	REPAIR HIATAL HERNIA	ESOPHAGOGASTRECTOMY
Good	Severe	2	25	
	Moderate	1	14	
	Minimal	5	19	
	All	8	58	
Fair	Severe	7	1	
	Moderate	3	1	
	Minimal	4	1	
	All	14	3	
Poor	Severe	6	3	2
	Moderate	2	1	
	Minimal	5		
	All	13	4	2

One patient lost to follow up

TABLE V TREATMENT OF ESOPHAGITIS WITHOUT HIATAL HERNIA

RESULTS	DEGREE	CONSERVATIVE TREATMENT	RECONSTRUCT CARDIAC SPHINCTER MECHANISM	ESOPHAGOGASTRECTOMY	REPAIR PERFORATION	JEJUNAL TRANSPOSITION
Good	Severe	4		1	1	1
	Moderate	2	5			
	Minimal	3	2			
	All	9	7	1	1	1
Fair	Severe					
	Moderate					
	Minimal					
	All					
Poor	Severe	2		3	1	
	Moderate					
	Minimal	1				
	All	3		3	1	

One patient lost to follow up

thoracic procedures. Peculiar to the operation of hiatal hernia repair in this series was the development of temporary dysphagia in a few patients postoperatively when none existed preoperatively. The dysphagia subsided spontaneously, and only occasionally was a single dilatation necessary.

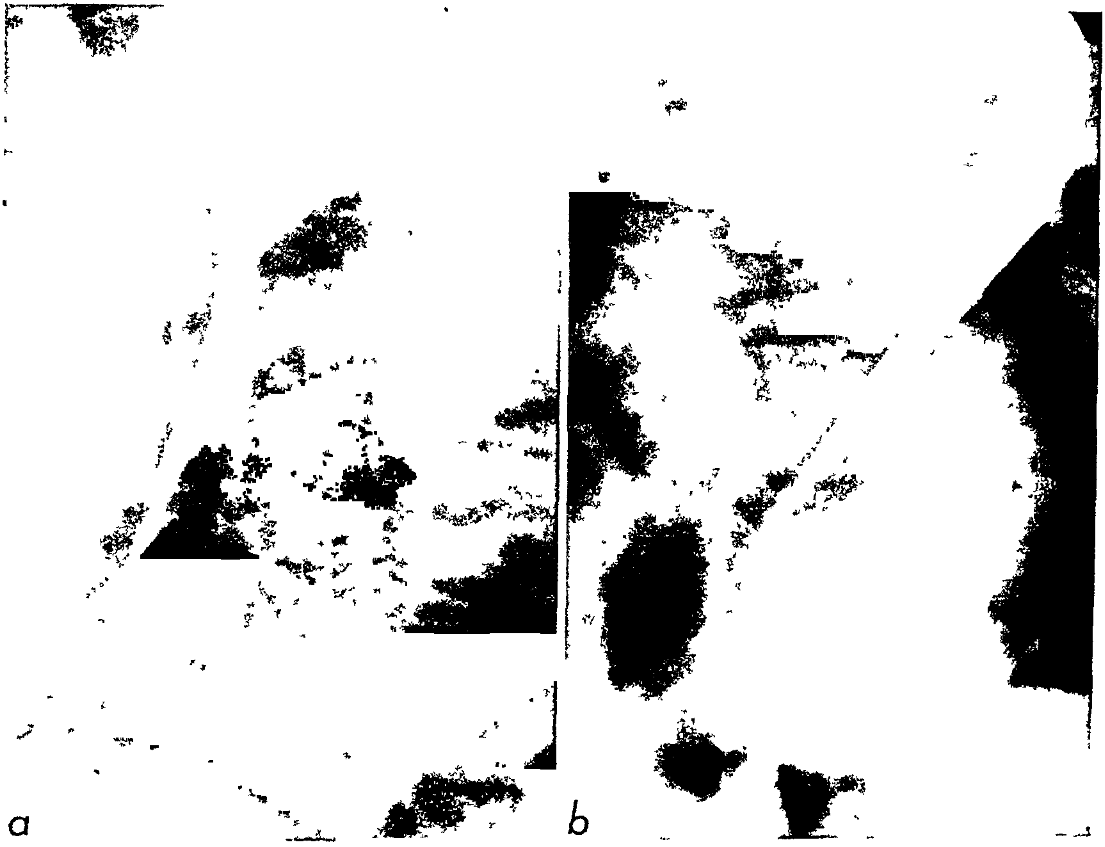

Fig. 3.—*a*, Esophagrams before treatment for esophagitis with stricture and hiatal hernia. *b*, After 2 years of medical therapy during which time thirty-seven esophageal dilatations were done Although the patient is relatively asymptomatic, there is little change in the x-ray appearance.

Of the 103 patients with a demonstrable hiatal hernia, 65 had hiatal hernia repair as definitive treatment for the associated esophagitis. The esophagitis in 29 of these patients was graded as severe, and 23 of these had a strictured or short esophagus. Sixteen patients had moderate esophagitis, and 20 had minimal esophagitis. The majority of the patients had significant symptoms, however, regardless of the demonstrable severity of the esophagitis. The results of surgery in terms of alleviation of prior symptoms, ability to eat all types of food, and absence of the need of special medication or treatment were good in 58 of the 65 patients with hiatal hernia repair. The results were fair in 3 (improvement, but not complete amelioration of symptoms), and poor in 4 (no change in symptoms in 3, and death in 1). The poor results occurred in 3 patients with severe esophagitis, and 1 with moderate esophagitis. Twenty-five of 29 patients with severe esophagitis were completely cured with the ability to eat types of food the ingestion of which for years previously resulted in intolerable symptoms. Patients with moderate or minimal esophagitis all had good or fair results with the exception of 1. It is interesting to note by way of contrast that in the 35 patients having esophagitis and an associated hiatal hernia treated medically, the results of treatment were good in only 8, fair in 14, and poor in 13. There were 15 patients with severe esophagitis in this group; 13 had fair or poor results, and only 2 had good results. The roentgenograms of one of the patients with a good result are shown in Fig. 3. This patient received 37 esophageal dilatations over a period of 2 years, has only slight dysphagia, and is receiving dilatations about every 6 months at present.

Two patients had esophagogastrectomy performed as the treatment of choice for esophagitis, early in our experience, with poor results. This operation would not be done at the present time.

Twenty-seven patients in whom no hiatal hernia could be demonstrated were treated for esophagitis (Table V). One patient was lost to follow-up, and 1 patient died following repair of a spontaneous esophageal perforation. Twelve patients were treated by the conservative means outlined previously, with good results in 9 and poor results in only 3. Four of 6 patients with severe esophagitis reported good results. Seven patients who had reconstitution of the cardiac sphincter mechanism as the treatment for their esophagitis will be discussed later. Four patients had an esophagogastrectomy, with a good result in only 1 and poor results in the other 3. One patient survived repair of a spontaneous perforation of the esophagus, and 1 patient died following this procedure.

In only one instance so far has a jejunal interposition procedure been done; this in a patient with long-standing esophagitis following a Heineke-Mikulicz cardioplasty for achalasia of the esophagus. The result has been outstandingly good. In the light of this experience, 2 other patients are being considered for this operation at the present time, one having had a previous esophagogastrectomy, and the other a Heineke-Mikulicz cardioplasty.

RECONSTRUCTION OF THE CARDIAC SPHINCTER MECHANISM IN PATIENTS WITH ESOPHAGITIS AND NO DEMONSTRABLE HIATAL HERNIA

Winkelstein,[22] in 1935 described peptic esophagitis as a new clinical entity, stating that the mechanism was not entirely clear. Since that time, a number of articles associating peptic esophagitis with herniation of the stomach through the esophageal hiatus have been published. In 1957, Winkelstein discussed peptic esophagitis associated with duodenal ulcer and differentiated it from that associated with a hiatal hernia, severe vomiting, esophageal intubation, previous operations on the esophagogastric junction, and that associated with persistent embryonic columnar epithelium. He reported 16 patients, 5 of whom had a small associated hiatal hernia. These he believed were secondary to traction of the stomach into the chest by a chronically inflamed esophagus. Such an esophagitis might be described as a "primary" or "true" peptic esophagitis, a part of an ulcer diathesis.

Whether an ulcer diathesis exists or not, there must be some explanation for the transcardial reflux of gastric juice. The most logical concept is the competency of the cardiac sphincter mechanism which exists most frequently

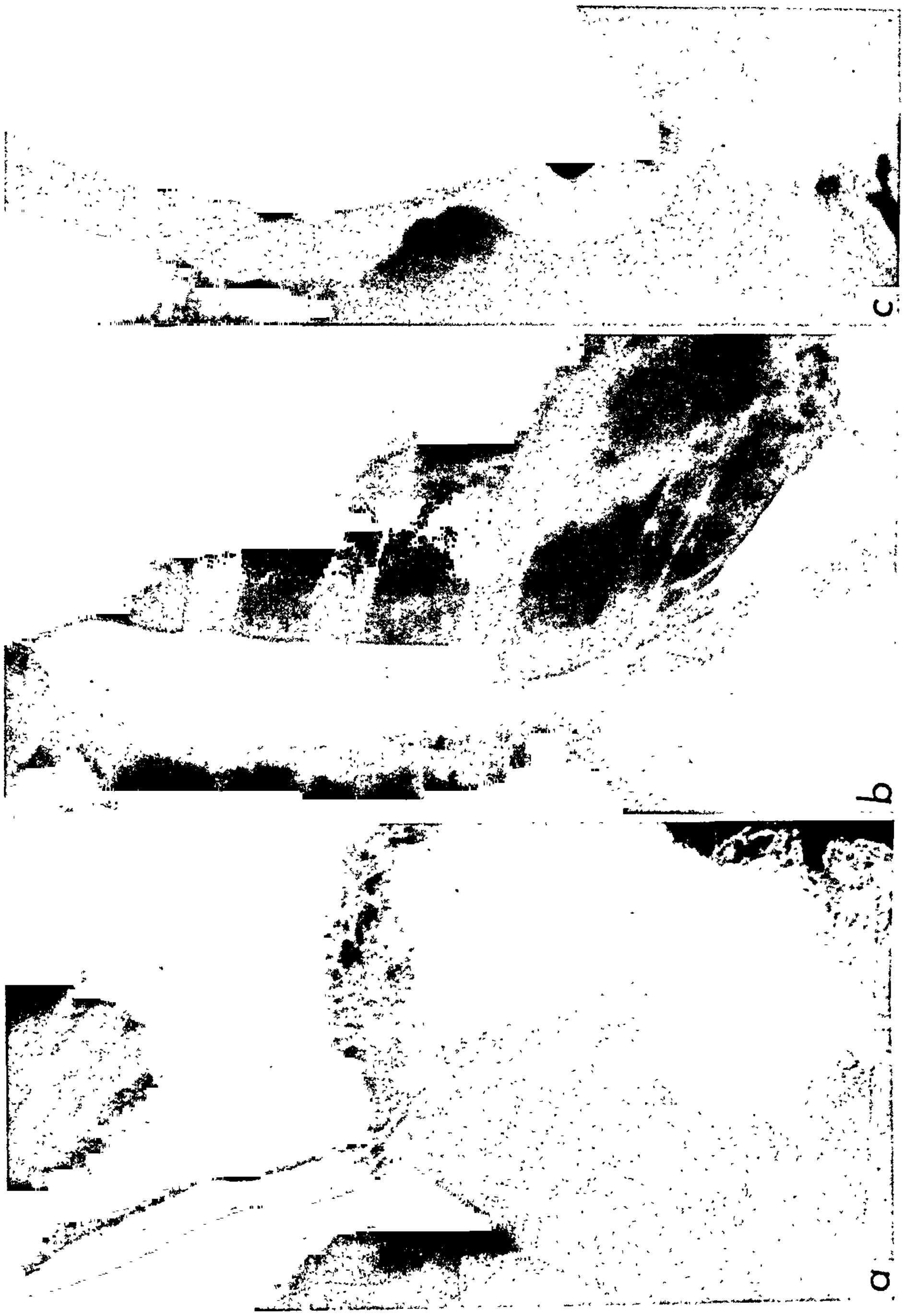

Fig. 4.—Roentgenograms of patients with esophagitis and no demonstrable hiatal hernia in whom reconstitution of the cardiac sphincter mechanism was done.

in association with a hiatal hernia It is well known that herniation of the stomach through the esophageal hiatus is frequently missed on routine upper gastrointestinal studies, and may be difficult to demonstrate even when special efforts are made In other instances, although no hiatal hernia is seen, it is possible to demonstrate regurgitation of barium from the stomach into the esophagus, indicating insufficiency of the cardiac sphincter mechanism There are at least 4 patients in the present series in whom a hiatal hernia was found only after repeated x ray examinations Furthermore, we have been intrigued on occasion by the fact that what has been considered a hiatal hernia by us has been interpreted and reported by the radiologist as a phrenic ampulla This discussion points to the conclusion that small undiscovered hiatal hernias, or at least an anatomic insufficiency of the cardiac sphincter mechanism, are responsible for many cases of so called "true" peptic esophagitis, and that if a small traction" hiatal hernia is present, it is likely the cause rather than the result of the esophagitis It should logically follow that certain patients with esophagitis in whom no hiatal hernia is demonstrated should benefit by reconstruction of the cardiac sphincter mechanism as in hiatal hernia repair Seven patients in the present study falling into this category of esophagitis with no demonstrable hiatal hernia were operated upon, and the cardiac sphincter mechanism was reconstituted in the usual manner The results of this procedure in all 7 patients were uniformly good Three case reports follow of patients who are typical of the group

Case 1—M B, a 37 year old white male laboratory worker, had had epigastric and substernal pain 14 years prior to admission The burning pain was aggravated by drinking alcoholic beverages, dietary indiscretion, smoking, and lying down after meals The pain was partially controlled for short intervals by diet and antacids X ray studies failed to show evidence of the presence of an esophageal hiatal hernia (Fig 4, *a*) The physical examination was not remarkable On Dec 12, 1958, esophagoscopy revealed a minimal chronic esophagitis with free regurgitation of gastric juice into the terminal esophagus Following this examination, reconstitution of the cardiac sphincter mechanism was done through a transthoracic approach At the time of surgery the esophageal hiatus was patulous, but no evidence of a hiatal hernia was seen The postoperative course was uneventful, and the patient was discharged on the ninth postoperative day He returned to work 2 weeks later and has been entirely asymptomatic to the present time on an unlimited diet containing foods that could not be ingested previously

Case 2—E D, a 35 year old white male steel worker, complained of substernal burning of 4 years' duration aggravated by lying down after meals and at night He had been on ulcer therapy with little relief for the first 2 years of his illness, and discontinued this therapy when he realized it was not helping Upper gastrointestinal studies in another hospital showed no evidence of a hiatal hernia, gastric, or duodenal ulcer On two prior hospital admissions esophagoscopy disclosed esophageal erosions in the terminal esophagus He entered the hospital for operation complaining of an increase in his symptoms for the previous 3 months Physical examination was noncontributory X ray studies again failed to demonstrate a hiatal hernia (Fig 4 *b*) Esophagoscopy disclosed minimal esophagitis with regurgitation of gastric juice At operation on April 22 1957, it was noted that the esophageal hiatus was patulous There was a minimal bulging of the stomach through the diaphragm His postoperative course was uneventful except for a hydrothorax on the left which cleared with a single aspiration He was discharged from the hospital on the thirteenth postoperative day He has been asymptomatic to the present time except for some residual chest wall pain

Case 3.—A. H., a 35-year-old white male salesman, was admitted to the hospital with a 9-month history of substernal distress and postprandial pain, particularly aggravated by alcoholic intake which was seemingly a necessary part of his job. Physical examination was noncontributory. At esophagoscopy on March 24, 1956, a moderate esophagitis with linear erosions was noted. X-ray studies at this time showed no evidence of an associated hiatal hernia (Fig. 4, *c*). He was placed on appropriate medical therapy with no satisfactory relief and he returned for operation on May 28, 1956. At operation the esophageal hiatus was lax, and a very small but definite hernia was seen. The postoperative course was satisfactory, and he was discharged from the hospital on the thirteenth postoperative day with complete relief of his symptoms. He has returned to his prior occupation as a salesman with no recurrence of symptoms to date.

Definite esophagitis of a minimal or moderate degree associated with visible reflux of gastric juice was confirmed in all these patients by esophagoscopy. At the time of operation, definite anatomic changes were noted in the region of the esophageal hiatus in all 7. These consisted primarily of relaxation of the muscles constituting the right crus of the diaphragm making the esophageal hiatus more patulous than normal. A small portion of stomach protruded through the hiatus into the chest in 4 patients. No visible evidence of herniation was present in the other 3. In spite of such minimal anatomic findings, all of these patients benefited from surgical reconstruction of the cardiac sphincter mechanism with complete alleviation of the preoperative symptoms.

DISCUSSION

An attempt has been made to present in specific terms what is thought to be the proper treatment of peptic esophagitis. Obviously, all therapy must have as its end the inhibition of the damaging effects of acid-peptic juice on the vulnerable esophageal mucosa. To accomplish this, such contributing factors as an associated duodenal ulcer, the presence of a hiatal hernia, or previous surgery at the esophagogastric junction must be assessed in the light of their specific contribution to the production of the esophagitis. It must be decided whether the esophagitis can be improved by simple neutralization of the regurgitant acid juices as with the usual medical therapy, whether the acid-peptic juice itself must be eliminated by destroying the secretory potential of the stomach as in extensive gastric resection, or, finally, whether correction of an abetting factor such as an associated hiatal hernia will be sufficient to prevent further esophagitis. If the esophagitis can be traced to a single initiating event such as an episode of severe vomiting, or the presence of a gastric tube during the postoperative period, in which the insult to the esophagus is not likely to be a continuous or repetitive one, conservative therapy may well be considered as definitive treatment. In instances of chronic esophagitis with a more insidious onset, every attempt should be made to demonstrate the presence of an associated hiatal hernia or incompetency of the cardiac sphincter mechanism. If the presence of a hernia is demonstrated, medical therapy has been unsatisfactory, in our experience, in that only 8 of 35 patients obtained good results. Contrariwise, patients without an associated hiatal hernia were treated fairly successfully by medical means. It is believed that the poor results in the former group are due to the continued presence of the hiatal hernia as an abetting factor. In spite of this, patients should always be given a trial of medical therapy prior to operation, not only because a few will respond satisfactorily, but also because in most instances there will be some regression of the esophagitis making the contemplated operation easier to accomplish.

In those instances in which the esophagitis is associated with a reducible hernia, it is generally accepted that repair of the hernia is the treatment of choice. However, some difference of opinion exists as to the proper treatment of those patients with a short or strictured esophagus associated with an irreducible hernia. Twenty-nine patients in the present series had severe esophagitis, and 24 of these had a stricture or short esophagus demonstrable by x-ray studies and confirmed by esophagoscopic findings. By employing the type of hernia repair described previously, it was possible to obtain good results in 20 of these patients, with poor results in only 3. One of the failures occurred in a patient whose symptoms were aggravated by a large alcoholic intake. In another, a previous gastrectomy for duodenal ulcer indicated the possibility of a rather intractable situation. In a third, death occurred postoperatively. It is truly remarkable to note the rapid regression of symptoms and signs of esophagitis once the esophagogastric junction is replaced below the diaphragm to break the vicious cycle of acid peptic irritation of the esophagus. In view of such satisfactory results with a procedure that neither changes the normal physiology nor the functional capacity of the upper gastrointestinal tract, extensive gastric surgery or plastic procedures on the esophagogastric junction do not seem justified as a primary therapeutic effort. There are exceptions to any rule, however. Instances in which the terminal esophagus is destroyed by chronic irritation and inflammation, to the extent that it must be resected occasionally exist.

There were 14 patients in the present series with evidence of a gastric or duodenal ulcer associated with a hiatal hernia, suggesting either an ulcer diathesis or the possibility of a gastric outflow obstruction as an additional abetting factor. In no instance was more than hiatal hernia repair necessary to obtain a good result in any of these patients, although in one a simple Ramstedt type pyloroplasty was contemplated.

Probably the most serious problems in treating esophagitis arise in those individuals who have a severe esophagitis resulting from previous surgery on the esophagogastric junction. Our attempts at treating esophagitis by esophagogastrectomy resulted in almost uniform failure, with continuation of the esophagitis. Our most successful experience with this problem recently has been with 1 patient in whom a jejunal interposition procedure was done with a result gratifying enough to encourage contemplation of the continued use of the procedure in 2 more patients in the near future. We favor this operation to that proposed by Ellis,[17] since the latter procedure leaves gastric mucosa in juxtaposition to that of the esophagus, which past experience has shown creates the potential for further esophagitis.[10, 15]

The technique of hiatal hernia repair to reconstitute the cardiac sphincter mechanism in certain individuals with intractable reflux esophagitis, in whom no hiatal hernia can be demonstrated, has been used with gratifying results. This may seem like a radical approach to the problem at first glance. However, if one concedes that peptic esophagitis is the result of regurgitation of acid-peptic juices from the stomach, accepts the well-known fact that a small hiatal hernia or reflux may be difficult to demonstrate roentgenologically, and accepts the satisfactory results obtained by the reconstitution of the cardiac sphincter mechanism as in hiatal hernia repair, then this approach to the treatment of peptic esophagitis without demonstrable hernia seems reasonable. The good results in 7 patients treated in this manner, all of whom had been on prolonged medical therapy prior to surgery, strengthens this contention.

SUMMARY

1. One hundred and thirty patients with peptic esophagitis are presented. One hundred and three had a demonstrable hiatal hernia, and in 24 no associated hernia was found.

2. Associated etiological factors, such as severe vomiting, the presence of a duodenal ulcer, or previous operations on the esophagogastric junction, are discussed.

3. Repair of the associated hiatal hernia, rather than one of the other more complicated procedures recommended recently, is suggested as the treatment of choice, even in those patients with stricture and shortening of the esophagus associated with an irreducible hernia.

4. As a new concept in the treatment of esophagitis, reconstruction of the cardiac sphincter mechanism as in hiatal hernia repair is suggested, even though no definite hiatal hernia has been demonstrated, in certain selected patients in whom long-term medical therapy has failed.

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Discussion

DR BEATTY H. RAMSAY, Santa Monica, Calif.—I would like to compliment Dr Cross on his paper, with which I take no exception

Recently, in reading a book about the Nautilus submarine, Dr Rickover was said to have interviewed officers and put them into precarious situations unexpectedly and asked them what they would do about it. One such time he told an officer that he had just been put on a lifeboat with 4 other men, only one of whom could live How could he talk the other 4 into allowing himself to be the survivor?

I was recently brought into a situation I had not experienced before with regard to esophagitis A 46 year old patient had never sought medical care, although for 4 years he had had severe obstruction on swallowing At the time he was seen he was unable to swallow it all and had lost 20 pounds of weight.

The barium study showed a marked constriction of the lower esophagus 4 inches above the cardia, and through this very little barium could pass An adequate study for hiatus hernia could not be made Esophagoscopy was perfectly normal as far as his obstructing lesion, but at this point there was a very rigid stenosis and dilatation was impossible. A No 20 bougie tip could be passed through into the stomach, but dilatation did not occur, and the bougie tip was tightly grasped There was no sign of esophagitis above this lesion at all.

We thought it could be malignant, but the 4 year history, of course, suggested an inflammatory etiology. An attempt was made to treat him by conservative methods so that a better study could be obtained He had never had any form of antacid therapy.

However, in the hospital, with all the help we could give him, he was unable to swallow even his saliva We were therefore in the position of having to do something about his dysphagia.

At surgery we did a linear esophagomyotomy in the Heller fashion, in order to determine the pathology. We obtained a biopsy of the entire thickness of the fusiform lesion from the external musculature down to and including the mucosa. The outstanding feature here was an eccentric lesion, 2 inches in length, where the pathology appeared to be edema within the muscle coat, with chronic and acute inflammation of the mucosa

In essence, there was fibrosis of years' duration with acute inflammation and ulceration No malignancy having been found, the question was, what to do? Should we do an extensive resection on this man who had never had any therapy before but who could not swallow?

There was an hiatus hernia sac present but nothing was contained therein.

All we did was suture the mucosa very carefully, leaving the muscle apart as in the typical Heller esophagomyotomy.

The esophageal lumen was now large enough to accommodate a No. 18 Levin tube and a finger; therefore it seems that the obstructing factor was in the muscle wall, mostly due to edema and was not mucosal constriction. There was no problem during the postoperative course. Relief of the mural obstructive factor by simple longitudinal myotomy, plus correction of the hiatus hernia or other primary cause, may prove to be effective treatment for inflammatory strictures of the lower esophagus and thus save these people from extensive surgical resection.

DR. MAX G. CARTER, New Haven, Conn.—I should like to congratulate the authors. I think they have done a splendid job, and I don't think they need to feel any temerity at all about suggesting surgery for the patient who has peptic reflux esophagitis, because we all know it is a bad disease.

I merely would like to make a suggestion which many of you know about, I am sure, for refining the methods of diagnosis in that group of patients in which hiatus hernia is not obvious. Most of us now have improved radiologic facilities because of the advances in cardiovascular surgery. Image amplification with cineradiography is very useful for study of the barium swallow. A moderate number of patients in whom the diagnosis of esophageal vestibule or ampulla would otherwise be made will be found to have very small short esophagus-type hiatus hernias. This I am sure is the group in which the authors found great improvement, although their radiologists were unable to demonstrate hernias by the traditional methods.

DR. ALFRED HURWITZ, Brooklyn, N. Y.—I would like to compliment Dr. Cross and his associates for a thought-provoking and lucid paper.

There is a law akin to Parkinson's law which I think can be applied to this problem: namely, that the success rate of any operation varies in inverse proportion to the number of operations that are currently employed. I think, however, that many of the operative procedures that have been devised have a good deal of efficacy, and with that in mind, during the past 2 years I have combined salient features of operations that have been employed in the past.

I hesitate to mention before this Society my preference for the transabdominal approach. Even in the obese patient, I have had little difficulty in exposing the diaphragmatic aperture. I prefer to do the repair in the manner described by Harrington. I find that I can reach the more caudal aspects of the aperture more easily by the transabdominal approach. In addition, exploration of the abdominal organs can be carried out and cholecystectomy can be performed if indicated.

Then I reconstitute the angle, an approach which Mr. Barrett has emphasized, by placing two or three sutures between the medial wall of the fundus and the left lateral wall of the esophagus. The fundus is then anchored to the undersurface of the diaphragm with several additional sutures.

If the patient has an elevated gastric acidity, a bilateral vagectomy is done at this time. A Heineke-Mikulicz pyloroplasty is performed in all instances. This procedure constitutes another reason for my preference for the abdominal approach. The pylorus is sutured in a transverse direction with interrupted silk sutures of the Gambee type, a method employed for many years by Weinberg of Long Beach.

Our series is too small and the follow-up period too short to be statistically significant but our results thus far have been most gratifying.

One final word, and that is that the iatrogenic complication of esophagitis, secondary to Levin tube intubation, can be eliminated by the use of gastrostomy tubes, and we are using them with increasing frequency.

DR. WILLIAM E ADAMS, Chicago, Ill—I would like to say just a word about a factor that has already been mentioned, namely the question of malignancy arising in these patients

We have recently reviewed 32 cases of the short esophagus type, in 8 of which there was a malignancy arising on the stomach side of the esophagogastric junction. I am sorry to add that in those patients that were treated longer than 2 years ago none lived longer than that time.

DR. CROSS (Closing)—I would like to express my appreciation to those individuals who discussed this paper, and I would especially like to re emphasize what Dr Carter stated about small hiatal hernias being present when they are not demonstrable by ordinary examination This is one of the important points of the presentation, that is, that small hernias may be present, although not demonstrated, and that such patients can be helped by hiatal hernia repair Our colleagues in internal medicine categorize these patients as having "true" or "primary" esophagitis, and treat them medically, frequently without too much success.

The second important point that I would like to re emphasize is that I think we have shown that even severe esophagitis can be treated successfully by surgical repair of the associated hiatal hernias, and that other ancillary procedures, such as drainage operations, vagotomy, etc, are not necessary, and they may even complicate the result

UTILITY OF A NEW PROCEDURE OF VALVULAR ESOPHAGOGASTROSTOMY IN CASES OF BRACHYESOPHAGUS AND STRICTURE: CLINICAL AND EXPERIMENTAL STUDIES OF CIRCUMFERENTIAL ESOPHAGOFUNDOPEXY

David H. Watkins, Ph.D., William R. Rundles, M.D. (by invitation), and Louis Tatom, M.D. (by invitation), Denver, Colo.

Regurgitation esophagitis and peptic ulceration at the esophagogastric junction is an important problem at the present time, despite extensive experimental and clinical investigations to elucidate the mechanisms of development of the lesion and despite ingenious suggestions for operative management.

Since Quincke[1] in 1879 inculpated the gastric digestive juices as being the principal agents producing esophagitis, a continuing, accumulating body of information tends to confirm this opinion. Esophagitis may be produced in rats by the simple expedient of pyloric ligation. Esophagitis has been produced by implanting gastric mucosa into the esophagus, and acute, experimental ulcers of the esophagus have been shown to be retarded in their healing in the presence of hydrochloric acid. The presence of esophagitis has been correlated with the regurgitation of acid peptic secretions.

The physiology of the cardia is still not completely explained. The different experimental investigations and clinical observations, however, suggest that this closing mechanism is dependent on several factors. Reflux is prevented normally in five ways:

1. By the oblique implantation of the esophagus into the lesser curvature of the stomach like the tip of a whistle, where the esophagus forms with the fornix of the stomach the acute angle of His. (The mucosal fold produced is called the valve of Gubaroff.)

2. By the muscle fibers of the stomach along the lesser curvature which lie like a sling surrounding the cardia. This loop of gastric muscle, just deep to the mucosa, which passes around the cardia and down each side of the lesser curvature helps maintain the angle of His at the incisura. The earliest description of this muscle comes from Thomas Willis of Oxford, who not only described the loop but showed it in a drawing dated 1674.

3. By the muscle fibers of the right crus of the diaphragm which stabilize and support the right border of the esophagus.

From the Professorial Surgical Unit and the Division of Surgery, Denver General Hospital.

Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April 21-23, 1959.

4 By the fact of a tonic action of the esophagus or of a sphincter muscle in the *region of the cardia, which is found in a state of permanent tonus* This has been a point of continuing argument between anatomists and physiologists, but in my opinion there is no clear cut evidence of such a sphincter

5 By another structure which exists in man to oppose the tendency for the cardia to pass into the posterior mediastinum when the diaphragm is relaxed in expiration This is the diaphragmatico esophageal membrane or elastic ligament, a modification of the abdominal aponeurosis of the diaphragm (and therefore relatively fixed at its origin¹), it bridges the esophageal hiatus and is inserted into the adventitia of the gullet as a membranous ring with upward and downward "cuff" extensions

Or, using another formula, these different groups of muscles and fascias serve essentially two functions to preserve or to exaggerate the acute angle of entrance of the esophagus into the stomach, and to close the lower end of the esophagus like a sphincter We have therefore a kind of valve action and a kind of sphincter action

The incompetence of the cardia and esophagitis associated with esophageal hiatal hernia are automatically corrected when the now fairly standardized methods for replacing the stomach below the diaphragm and correcting the hiatal defect are applied What are these principles to be applied to the surgical repair of an ordinary sliding esophageal hiatal hernia in which the esophagus has its normal length (as determined by esophagoscopy) and in which the stomach can be easily replaced within the abdominal cavity? (1) Reduce the hernia to prevent reflux (2) Diminish the size of the esophageal hiatus to prevent recurrence of the hernia (3) Reconstitute the esophagogastric angle by fixing the cardia below the diaphragm and by diaphragmatico fundopexy to allow the fundus to balloon up under the dome of the diaphragm

In cases of esophageal hiatal hernia in which peptic ulcer has progressed to stricture formation and where the stricture is tough, fibrous, and incapable of dilatation to full caliber, more complicated therapy is indicated In these cases, the cardia and affected esophagus must be resected and the digestive continuity re established The operation of Wangensteen may be performed by resecting the entire acid bearing area of the stomach, and creating an esophago antral anastomosis with an extramucosal pyloromyotomy The difficulty with this operation is the loss of the gastric reservoir The operation of Allison may be recommended in certain cases Here, following a subtotal gastrectomy which leaves only the gastric antrum, continuity is re established by an esophagojejunostomy with the Roux en Y The criticism of this procedure is the absence of the gastric reservoir, and short circuiting of the *duodeno pancreaticobiliary block* Recent studies have suggested that the interposition of an isoperistaltic segment of jejunum ileum, or colon between the esophagus and stomach may prevent regurgitation of gastric or duodenal contents into the esophagus and hence avoid esophagitis

While these methods are all extremely useful in given situations, it would appear that a technique which would allow resections of strictures of the lower third of the esophagus together with preservation of the stomach by a simple

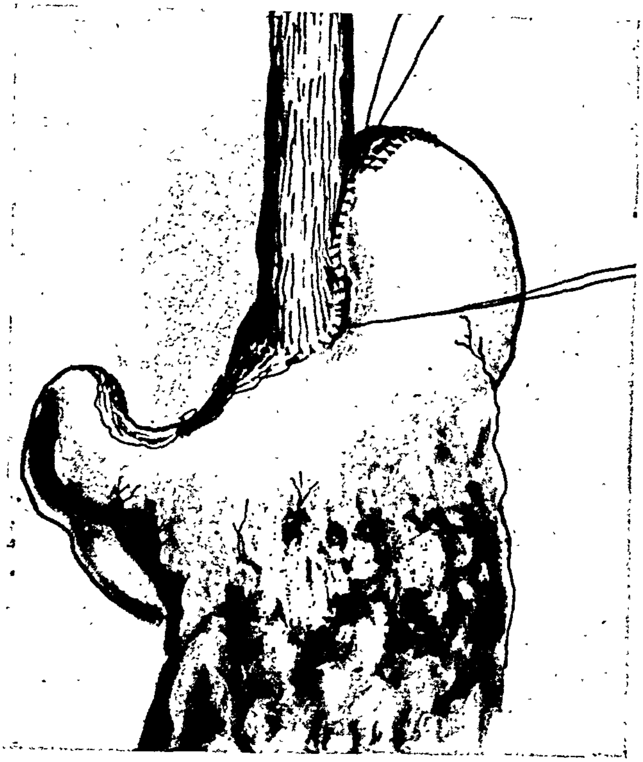

Fig. 1.—The esophagogastrostomy has been completed, and the left border of the esophagus is being approximated to the lesser curvature of the fundus superior to the esophagogastrostomy.

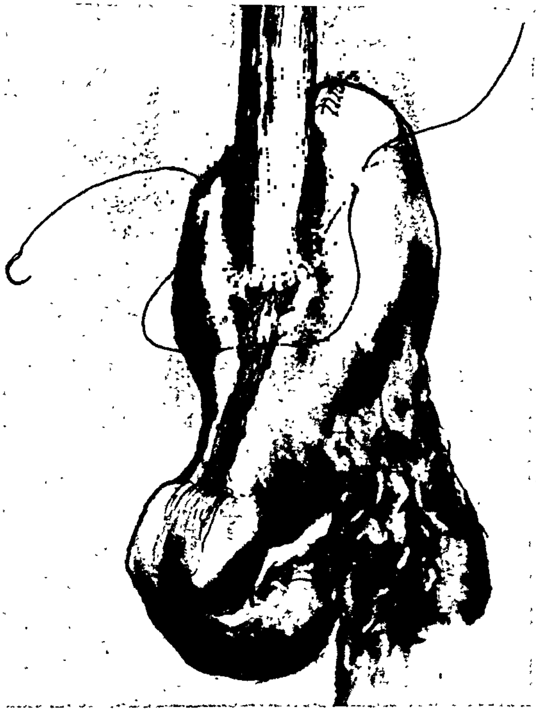

Fig. 2.

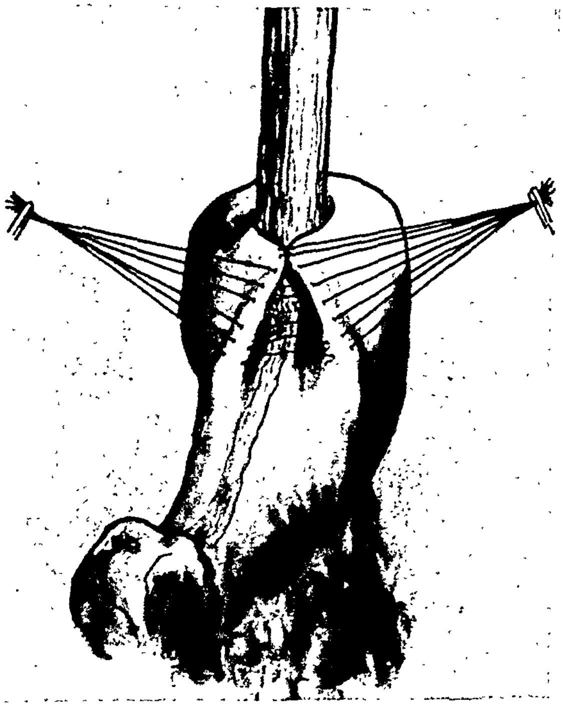

Fig. 3.

Fig. 2.—The first step in performing circumferential esophagofundopexy consists of creating a Witzel type tunnel for the esophagus by approximating the anterior and posterior walls of the stomach with interrupted sutures.

Fig. 3.—The sutures placed to form the circumferential esophagofundopexy are being tied.

surgical technique would be much preferable because these lesions are frequently found in old, debilitated, starved people. Thus, our attention was drawn to investigation of a simple method by which esophagogastrostomy would be performed in such a fashion that reflux esophagitis would be prevented.

MATERIALS AND METHODS

I. Fifteen adult mongrel dogs were prepared. The abdomen was opened through a left rectus muscle retracting incision, and the fundus of the stomach was resected, making certain that the sling muscle passing around the esophagogastric junction at the angle was completely interrupted The stomach wall was sutured, utilizing two layers of sutures

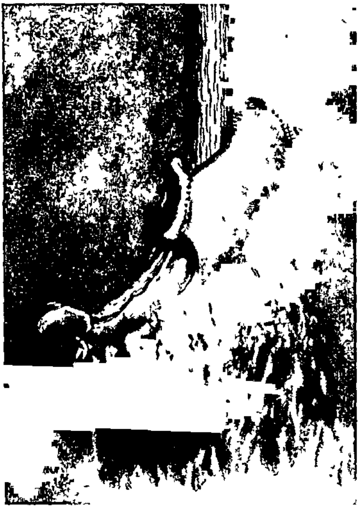

Fig 1.

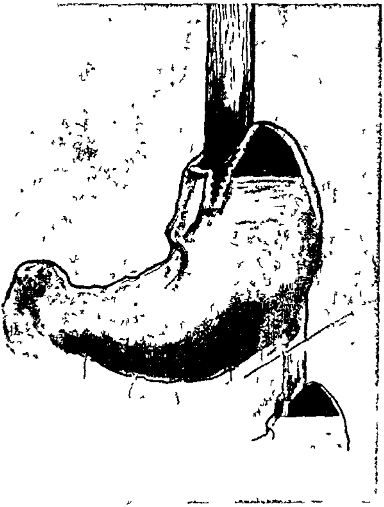

Fig 5

Fig 4—The completed appearance of the esophagofundopexy is well shown The approximation of the anterior and posterior walls of the stomach must extend well below the *junction of the esophagus and stomach*

Fig 5—Frontal section showing the disposition of the esophagus with relation to the wall of the stomach and the magenblase The insert shows the approximation of the esophageal *walls at the position of rest (absence of swallowing)*

II. Ten dogs were prepared for controls by placing the cardioesophageal junction above the diaphragm by interrupting the diaphragmatico-esophageal membranes, and thus creating a sliding type of esophageal hiatal hernia. These animals were observed over a period of 18 months. The edges of the hiatus were sown to the prolapsed stomach with interrupted silk sutures. In a few cases the hiatus required enlargement by an incision through the hiatal ring.

III. Twenty dogs were prepared as follows. Through a left transthoracic incision the esophagus was identified, the esophageal hiatal ring was incised in a radial direction for 2 to 3 cm., and the stomach was drawn up into the left pleural cavity. The cardioesophageal angle was reconstructed above the diaphragm by approximating the medial border of the gastric fundus to the left border of the esophagus with a row of interrupted sutures of 3-0 silk for a distance of 5 to 10 cm. from the cardioesophageal junction (Fig. 1). With the angle thus reconstructed, circumferential esophagofundopexy was carried out. The anterior and posterior surfaces of the fundus are wrapped around the distal esophagus for a distance of 4 to 6 cm. and approximated by interrupted silk 3-0 sutures to produce in essence a Witzel tunnel (Figs. 2, 3, 4, 5).

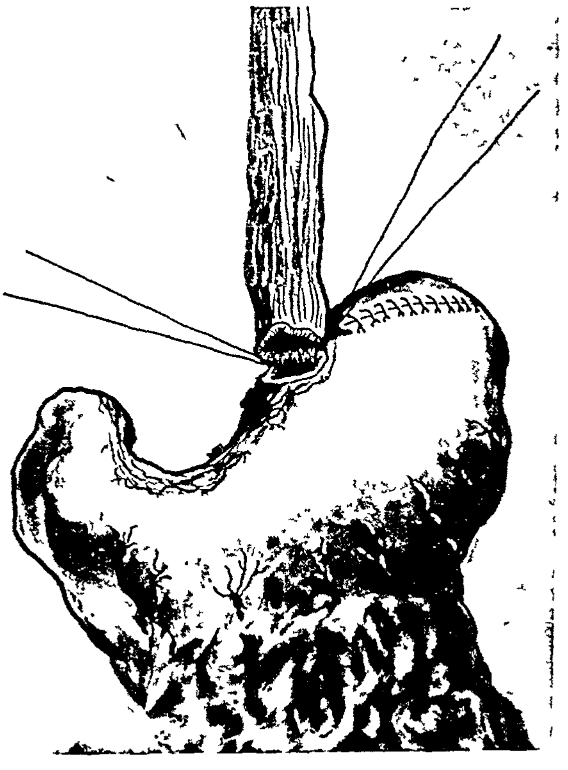

Fig. 6.—A stricture involving the lower third of the esophagus has been excised, and the inosculation of the esophagus into the cardia has been obliterated by suture. An esophagogastrostomy is being performed on the lesser curvature.

Thus, the esophagogastric junction, angle, and Witzel tunnels were left in the left pleural cavity with the diaphragm loosely sutured to the stomach below. The diet was gradually increased from fluids to full kennel ration.

In 10 dogs the same plan of procedure was carried out except that the distal 4 cm. of esophagus were resected and esophagogastrostomy was carried out (Fig. 6) utilizing the same plan of circumferential esophagofundopexy. Dogs with these esophagogastric anastomoses received nothing by mouth for the first 3 postoperative days.

Esophagoscopy was routinely performed under Pentothal anesthesia preoperatively, 4 to 6 weeks postoperatively, and at intervals thereafter until the animal was sacrificed. After the first esophagoscopy, a nasogastric tube was placed into the stomach and 200 c.c. of a thin barium suspension was injected. Reflux was determined by fluoroscopy, utilizing a tilt-table in the Trendelenburg position and manual pressure on the abdomen.

IV. Fifteen normal fresh postmortem human esophagi and stomachs were studied. The pylorus was cannulated and the stomach was distended with water from a reservoir which was raised alongside a measured rule until the water was seen to escape from the esophagus. These experiments were carried out with the fundus of the stomach in different positions in the body and following removal from the body. In six stomachs a sham operation was performed obliterating the angle of His initially and then carrying out circumferential esophagofundopexy (Fig. 7). Studies were made observing regurgitation following cannulation of the pylorus, and roentgenographic studies were carried out utilizing thin suspensions of barium and distention of the stomachs with air.

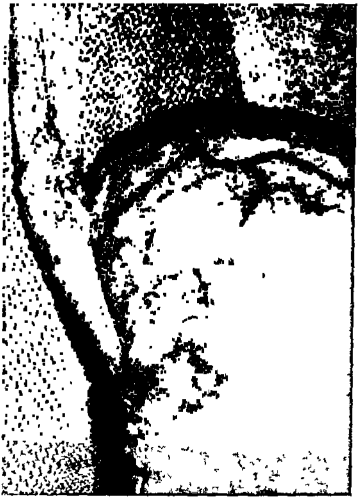

Fig 7.—Appearance of esophagofundopexy performed on the esophagus and stomach removed from a cadaver.

RESULTS

In the group of animals in which fundusectomy was carried out, and in which the loop of Willis remained intact, no esophagitis developed over a period of 12 months. On the other hand, in those animals in which the loop of Willis was interrupted during the fundusectomy, esophagitis appeared promptly, usually within 4 to 6 weeks.

Peptic esophagitis does not develop so regularly following the production of an experimental hiatal hernia by drawing two thirds of the stomach into the thorax and fixing it to the cut edges of the diaphragm by suture as it does following esophagogastrostomy or by surgical excision of the left crus of the canine diaphragm (which is comparable to the right crus of the human diaphragm) and allowing a cardiac incompetence to develop gradually. The development of esophagitis may be hastened by obstruction of the superior gastric loculus. In any case, however, evidence of peptic esophagitis developed within 9 months in three quarters of these animal preparations.

The series of dogs which had been prepared by circumferential esophagofundopexy showed no evidence of peptic esophagitis when they were observed over a period of 36 months. During esophagoscopy in these animals slight to moderate resistance was encountered in the distal esophagus. With slight pressure the esophagoscope passed through this area, and its passage was sometimes followed by escape of gas or fluid. All of these animals demonstrated competency with the barium studies, whereas the hiatal hernias all exhibited reflux. However, very little pressure was required to inject the thin barium contrast medium through the esophagi into the stomachs of anesthetized dogs which had had this operative procedure.

Our pressure injection experiments confirmed the importance of the mechanical arrangement of the fundus which, when it is excluded from the lumen of that viscus, diminishes greatly the resistance offered by the cardia to regurgitation. When the left leaf of the diaphragm was removed to allow the fundus to protrude into the left pleural cavity unhindered, the pressure necessary to induce regurgitation was increased. The liver tunnel, the crura of the diaphragm, and the pressure of the surrounding viscera are important in maintaining the relationship of the fundus to the body of the stomach and the esophagus and the efficiency of the cardioesophageal angle.

The procedure of approximating the right border of the fundus of the stomach to the left border of the esophagus by a row of interrupted sutures increases the resistance of the cardia to regurgitation only if the stomach and esophagus remain in their relative normal positions within the abdomen. If this same preparation is carried out on the isolated esophagus and stomach, pressure applied through the pylorus produces bulging of the right wall of the esophagus and offers no hindrance to regurgitation. In the normal body, however, the crura, the liver tunnel, and other surrounding structures buttress the right border of the esophagus so that the angular mechanism is efficient.

Pressure regurgitation studies carried out on the isolated esophagus and stomach which had been subjected to circumferential esophagofundopexy showed maintenance of competency even though the entire preparation had been removed from the body (Fig. 8). This is illustrated in Fig. 9 in which the stomach and esophagus have been coated with a thin barium suspension and air has been introduced through the pylorus. The competency of the cardiac valve is seen.

CLINICAL APPLICATIONS

Since the primary pathologic feature in reflux esophagitis is an incompetent cardiac sphincter, the development of esophagitis with its several complications is a secondary phenomenon consequent to sphincter relaxation. Causal therapy

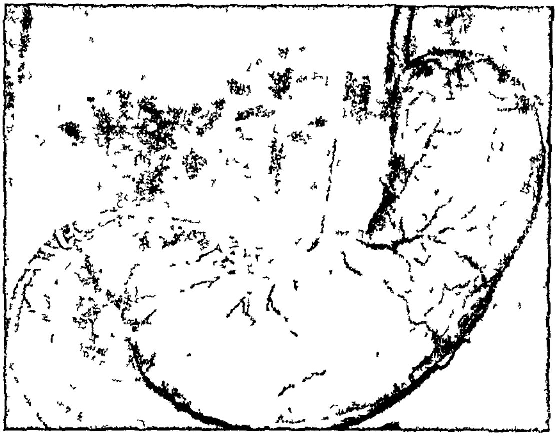

Fig 8 —The stomach upon [illegible] has been performed has been
grossly distended with air injected [illegible] through the pylorus Note the
competence of the circumferential [illegible] which allows no air to pass
from the stomach into the esophagus

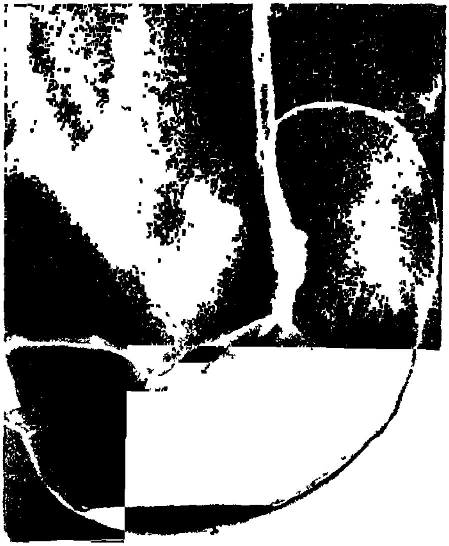

Fig 9 —Note the patency of the lumen of the esophagus [illegible] suspension is passing from the esophagus into the stomach [illegible] pexy appears rather [illegible] the lumen in the [illegible]

therefore must be directed to the sphincter mechanism itself. Regurgitation and belching are common physiologic events in normal men and dogs, and they demonstrate that the cardiac mechanism is a reversible one which may be at times incompetent normally. Thus, the simple reflux of gastric chyme is no indication for therapy. This reflux of gastric content may occur with and without esophageal hiatal hernia, and with or without the serious complications of esophagitis. Thus, the procedure would certainly not be considered in patients with reflux esophagitis associated with sliding hiatus hernia which is readily curable by conventional methods of hiatal repair. The procedure which we are considering is suggested only in patients with the serious complications of esophagitis, such as stricture and/or ulceration, hemorrhage, and perforation. Esophagitis occurs frequently in patients with congenitally short esophagus.

Reflux esophagitis is not a single pathologic entity but a group of conditions of probable common origin. Despite the severity of the disease processes in some cases, the inflammatory process may be remarkably superficial. It is common for inflammation and scarring to penetrate the submucosa, even when a marked stricture is present. In these cases rapid epithelial healing follows reduction of the acid gastric secretions which are regurgitated into the esophagus. For the small number of patients who have extension of the inflammatory process into the muscular tunic, the prognosis is less favorable.

In cases of sliding esophageal hiatal hernia with secondary short esophagus, two situations present themselves. In the first case, the esophagus can be dilated readily to good and sufficient caliber. Here we believe transthoracic circumferential esophagofundopexy with no attempt to reduce the stomach below the diaphragm should be carried out. Occasional esophageal dilatations may be required. In cases of esophageal hiatal hernia in which the peptic ulcer has progressed to stricture formation and in which the stricture is tough, fibrous, and incapable of dilatation to full caliber, we believe that distal esophagectomy extending above the stricture with repair by esophagogastrostomy and circumferential esophagofundopexy is the procedure of choice.

ILLUSTRATIVE CASES

R. B. was born in December, 1948, a full-term infant with normal development. His mother's history and pregnancy were not remarkable, and he weighed 6 pounds at birth. In June, 1949, he had a 2-week episode of hematemesis and vomiting; however, he ate with a good appetite. In July, 1949, he was admitted to the Pediatric Ward of the Denver General Hospital for recurrent intermittent hematemesis. He had failed to gain weight and vomited once daily. His gastrointestinal series at this time was considered to be normal. Following his hospitalization there was no blood in the vomitus, raised on an average of once daily for 1 month. In September, 1949, he again had recurrent hematemesis and daily spells of crying. Esophagoscopy at this time showed blood emerging from the cardia of the stomach, but no definite lesions were seen. Exploratory laparotomy was carried out with abdominal repair of a diaphragmatic hernia, appendectomy, and gastrotomy. The latter procedure demonstrated no gastric lesions. At this time he was considered to have a congenital short esophagus. The postoperative course was satisfactory.

Following this operation he had attacks of recurrent vomiting, the vomitus often containing blood and associated with some abdominal pain. He continued to eat well and to have a good appetite. In March, 1950, he was again hospitalized with severe recurrent hematemesis and anemia. A second exploratory laparotomy and gastrotomy at this time demonstrated no site of bleeding. Fig. 10 shows an esophagram taken in February, 1952. In May, 1953, he was again admitted to the hospital with abdominal cramping pain, recurrent hematemesis, and vomiting. Esophagram at this time showed gastric mucosa in the lower thorax, but no gastric pouch or stenosis was noted. Esophagoscopy demonstrated an intrathoracic stomach with terminal esophagitis, and bleeding from the lower esophagus. On June 1, 1953, a left phrenic nerve crush was performed.

On June 5, 1953, a third laparotomy was carried out with repair of a recurrent diaphragmatic hernia. Postoperatively he had continuous nasogastric suction, and the course was uncomplicated. Between June, 1953, and March, 1954, he had occasional hematemesis and intermittent abdominal and substernal pain. His weight varied between 30 and 35 pounds without appreciable gain. In March, 1954, he again had severe hematemesis and abdominal pain which persisted after antacids and milk for the next 2 months. Melena was present for 1 month. In May, 1954, a barium swallow showed a sliding esophageal hiatus hernia with gastric mucosa above the diaphragm and gastric retention. Esophagoscopy showed esophagitis of the lower third with bleeding at the cardia. A left transthoracic repair of the diaphragmatic hernia was attempted and incidental splenectomy and esophagorrhaphy were carried out. He made an uncomplicated recovery from this operation. In June, 1954, an esophagram showed no stricture at the esophagogastric junction. In February, 1955, he had a 1 week episode of abdominal pain, hematemesis, but

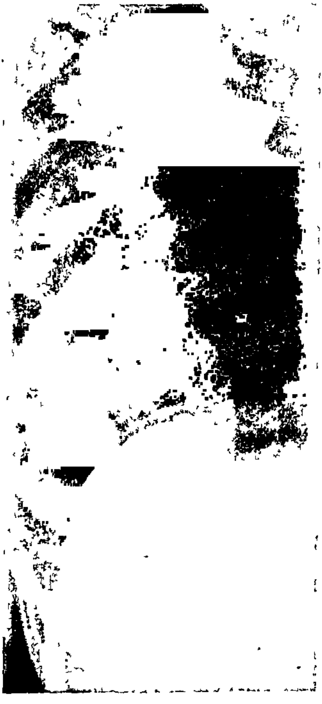

Fig. 10.—R. B. (Case 1). February, 1952. Esophagogram demonstrating short esophagus and recurrent esophageal hiatal hernia.

no melena. The hemoglobin at this time was 9 grams per cent, and stools were negative for blood. He weighed 35 pounds, and was placed on iron therapy. An esophagram demonstrated no hernia. Between February, 1955, and April, 1958, he had several upper respiratory infections with vomiting and some abdominal pain. His last hematemesis occurred in December, 1955. He slept with his head elevated and was taking multiple feedings. His weight had increased to 45 pounds. In April, 1958, he complained of marked tiredness in the morning and heartburn. His hemoglobin at this time was 9.8 grams per cent with 2.1 per cent reticulocytes. He was continued on iron therapy. In May, 1958, his stool guaiac was 4+ positive and hemoglobin was now 11.7 grams per cent. In July, 1958, an upper gastrointestinal x-ray series showed marked gastric reflux into the lower three quarters of the esophagus (Fig. 11), and a sliding esophageal hiatus hernia was seen.

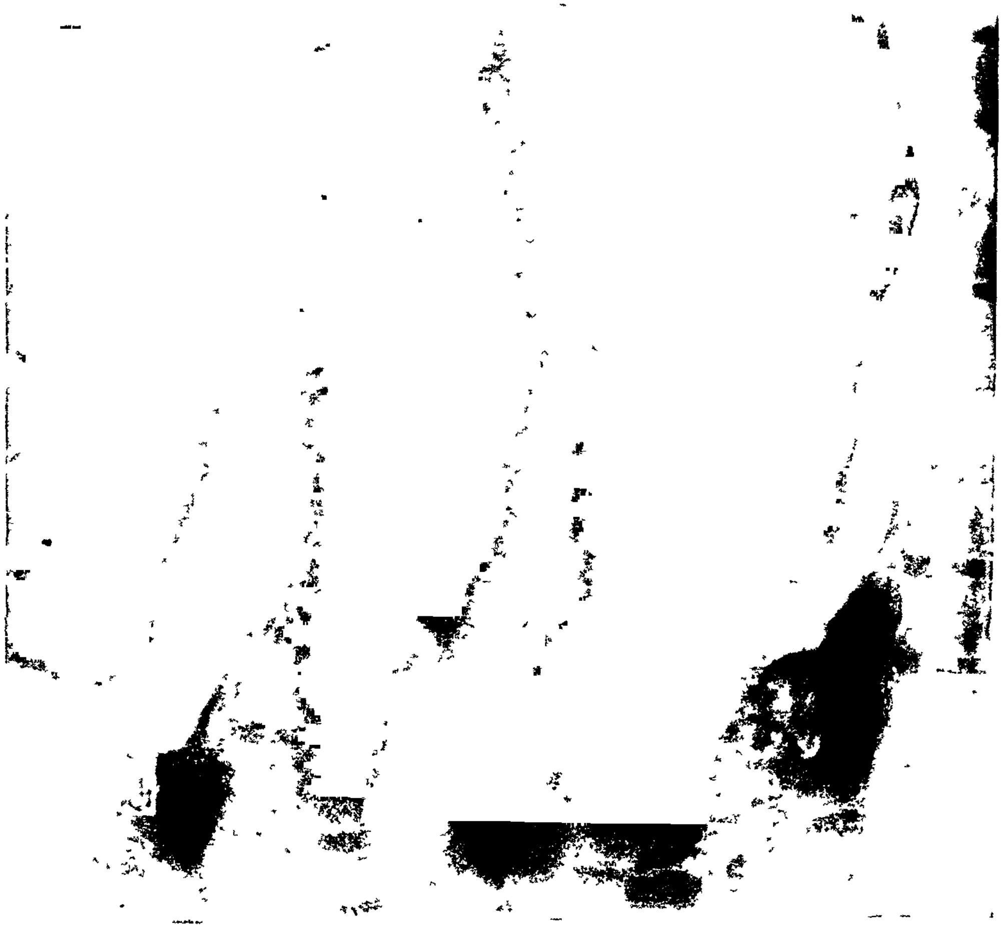

Fig 11.—R B. (Case 1). July, 1958 Massive reflux of barium into the esophagus demonstrated by placing the patients in the Trendelenburg position following a barium meal.

There was some pylorospasm present. Esophagoscopy demonstrated an esophageal ulcer at 27 cm. with fresh bleeding and marked esophagitis. Gross incompetence of the cardia was present. X-ray studies in August, 1958, showed the magenblase above the left diaphragm (Fig. 12).

In September, 1958, left thoracotomy was performed. At operation 8 cm. of stomach were present in the posterior mediastinum. The lower third of the esophagus was markedly thickened, edematous, and attached to the subpleural connective tissue by rather dense, friable adhesions. However, since preoperative esophagoscopy had demonstrated that the esophagus could be easily dilated to full caliber, it was decided to perform circumferential esophagofundopexy without resecting that portion of the lower third of the esophagus which was obviously the site of esophagitis. The gastric pouch was separated from the diaphragmatic orifice to which it was attached by firm adhesions so that the stomach could be more easily drawn up into the thorax. A line of sutures of interrupted 3-0 silk were placed between the left border of the esophagus and the right border of the gastric fundus for a distance of 6 cm. Then the posterior and anterior surfaces of the fundus of the stomach were wrapped around the distal third of the esophagus and approximated snugly with two layers of interrupted 3-0 silk sutures. This layer of sutures was continued to a point 2 cm. below the inosculation of the esophagus into the gastric cardiac so as to protect the squamous epithelium of the cardia from the acid-pepsin gastric juice. The stomach was then anchored to the esophageal-diaphragmatic orifice with interrupted 3-0 silk sutures. Following the placement of two intercostal chest tubes, the chest wall was closed in layers. An indwelling nasogastric tube had been placed in the stomach preoperatively, and this was allowed to remain until the third postoperative day. He made an uncomplicated recovery and has had no attacks of hematemesis since that time. Postoperative chest film shows a gas bubble posterior to the heart. His weight was 45 pounds at discharge.

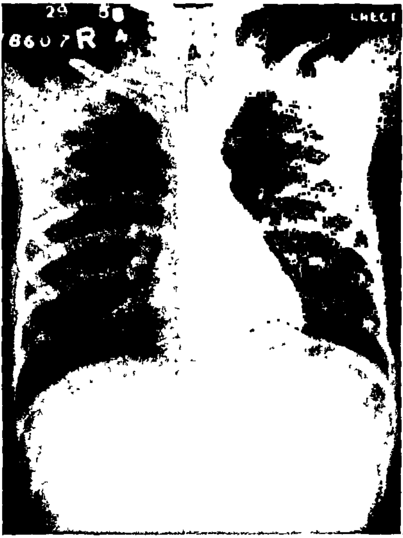

Fig 12.

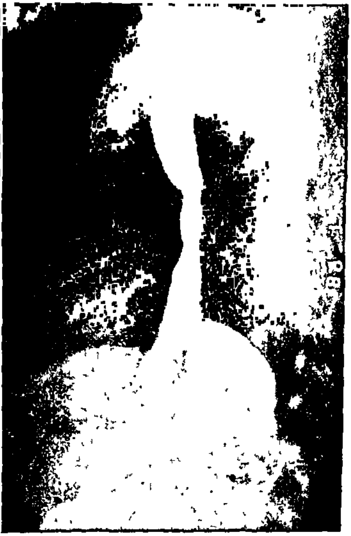

Fig. 13

Fig. 12.—R B. (Case 1). Aug 29, 1958. The magenblase is well seen above the left diaphragm, indicating an esophageal hiatal hernia.

Fig 13.—R B. (Case 1). Dec 1, 1958. Postoperative upper gastrointestinal series shows the esophagus and stomach during the act of swallowing a large bolus of barium. The extent of the Witzel tunnel is demonstrated, and the barium is seen to enter the stomach readily.

In December, 1958, an esophagram demonstrated no reflux with the patient in a marked Trendelenburg position. The cardia was seen to fill above the diaphragm, and there was no dilatation of the esophagus (Fig. 13). In January, 1959, esophagoscopy demonstrated no esophagitis and no reflux in the supine or Trendelenburg position. There was good closing of the terminal esophagus. At this time the hemoglobin was 15.4 grams per cent, and he weighed 48 pounds. In March, 1959, an esophagram demonstrated no esophageal reflux or stricture.

Comment: This boy had been subjected to four attempts to repair what is obviously an esophageal hiatal hernia of the congenital short esophagus type with recurrent ulcerative esophagitis. In spite of repeated efforts to place the stomach below the diaphragm, the shortening of the esophagus was such that this maneuver could not be accomplished, and the hernia promptly recurred. He had suffered from recurrent ulcerative esophagitis with hematemesis since his nursling days and had received only moderate amelioration by any of the procedures which had been carried out. Recognition of the fact that esophagitis was the serious component of this patient's lesions, and dispossessing ourselves of the preoccupation to produce anatomic restoration of the concerned viscera, we felt that this boy presented an ideal indication for trial of our investigative circumferential esophagofundopexy. His prompt and gratifying response to this procedure gives us encouragement, although repeated long-term observation will be necessary to establish the worth of this undertaking.

M. K., a 62-year-old white waitress, had been seen in the Medical Outpatient Department from May of 1956 to January of 1957. She noted abdominal epigastric, and sometimes sharp substernal aching pains which had begun about 7 years previously, with recurrences of this pain at frequent intervals since that time. The pain was aggravated by lifting, stooping, straining on exertion, and by the ingestion of milk. The pain was lessened or decreased by the use of phenobarbital, retirement to bed with a hot water bottle, or discontinuance of activity. Pain was not related to meals; walking did not accentuate it. There was no associated nausea, vomiting, melena, or hematemesis. There was occasional radiation of pain into the back. Her weight had remained stable at 100 pounds.

Back pain associated with stiffness and soreness had been diagnosed as arthritis with response to appropriate therapy. She had had an appendectomy in 1929. A symptomatic right renal stone had been diagnosed in 1950 with abdominal ureterolithectomy in 1952 without relief of all symptoms. She had no frank pyelitis, but urinary frequency. Two gall bladder series taken 1 year prior to her first visit to Denver General Hospital were reported normal. Examination disclosed blood pressure to be 124/70 mm. Hg, pulse was 76 and regular, respirations were 16, and she weighed 102 pounds. Two healed scars were present in the right lower quadrant, and there was mild right lower quadrant tenderness which was superficial.

Laboratory examinations showed that hemoglobin was 14.9 grams per cent, total leukocyte count was 9,800 with a normal differential. Urinalysis was negative. Blood urea nitrogen was 8 mg. per cent; uric acid, 5.5 mg. per cent; fasting blood sugar, 107 mg. per cent. An electrocardiogram was negative. The gall bladder series showed a normal functioning gall bladder without stones. An upper gastrointestinal series showed a moderate-sized hiatus hernia with one fourth of the stomach above the diaphragm. The cervical and lumbar spine films showed osteoporosis with hypertrophic changes. An intravenous and retrograde pyelogram showed kinking of the right proximal ureter due to previous surgery without obstruction to the pelvis of the kidney and no dilatation of the ureter.

The patient was treated following her first visit with phenobarbital and belladonna. There was no relief of pain. She was seen over the next 5 months in several medical clinics with the same problem of abdominal pain. She was placed for a time on Peritrate and nitroglycerine without relief of pain.

In January, 1957, she was referred to the Department of Surgery and admitted to hospital. On Jan. 4, 1957, esophagoscopy showed redundant distal esophageal folds with a red, granular, friable bleeding mucosa without gross ulceration. No stricture was noted.

On Feb 11, 1957, this patient had repair of a sliding esophageal hiatus hernia by the left thoracic approach Over half of the stomach was present in the posterior mediastinum and, despite considerable mobilization of the stomach and esophagus, the stomach could not be reduced below the diaphragm Despite the fact that there was no concentric narrowing of the distal esophagus, it was believed that the protracted bouts of peptic esophagitis which she had experienced had produced longitudinal shortening of the esophagus Consequently, circumferential esophagofundopexy was carried out in the manner described above Following this, two thirds of the stomach was reduced below the diaphragm leaving one third, including the esophagogastric junction, in the posterior mediastinum The postoperative course was uneventful, and the patient was discharged on the eleventh postoperative day Subsequent clinic visits have shown her to be in good health with no further abdominal symptoms, and no evidence of peptic esophagitis This clinical impression has been verified by repeat esophagoscopic examinations

Comment This patient had developed incompetence of the gastric cardia secondary to the long standing esophageal hiatal hernia The regurgitative peptic esophagitis which then developed had resulted in damage only to the esophageal mucosa insofar as concentric narrowing is concerned However it was obvious at the time of operation that there was shortening of the esophagus in a longitudinal direction In those cases in which the esophagus can be dilated to full and sufficient caliber, we have been performing circumferential esophagofundopexy to control the peptic esophagitis and have not resected the distal esophagus Resection of the lower third of the esophagus has been reserved for deep strictures which could not be dilated

J W, a 76 year old white male old age pensioner, entered Denver General Hospital on May 10, 1958, with the complaint of dysphagia for 4 years and regurgitation of food for 1 month He had developed progressive increase in dysphagia during the preceding month and had lost 20 pounds in weight During the month preceding admission he had been unable to swallow any solids, and upon admission he was unable to take even water

Examination disclosed a poorly nourished, moderately well developed white man who appeared chronically ill Blood pressure was 110/75 mm Hg, pulse 84, respirations 24 Examination of the chest showed some increase in anteroposterior diameter The lungs were hyperresonant and the breath sounds were decreased in intensity A systolic murmur was present over the apex The remainder of the physical examination was not remarkable

The urinalysis was negative on admission Examination of the blood demonstrated a hemoglobin of 11 grams, white blood count was 12,400 with a normal differential Total blood proteins and the albumin globulin ratio were normal The serology was negative An electrocardiogram showed normal sinus rhythm with some enlargement of the left ventricle A roentgenogram of the esophagus showed a marked obstruction in the lower third at a point 8 cm proximal to the cardia

Esophagoscopy demonstrated an obstruction in the lower third of the esophagus The obstruction consisted of very firm, yellow, dense tissue which grossly appeared to be granulation tissue This impression was confirmed by microscopic examination

On May 19 1958, a left thoracotomy was performed through the bed of the eighth rib The lung showed chronic fibrosis and emphysema with a few scattered subpleural blebs The posterior mediastinum was opened and the lower third of the esophagus was found to be densely adherent to the surrounding cellular tissue and lymph nodes Approximately 8 cm of stomach was present above the diaphragm in the posterior mediastinum The esophagus was freed from its bed with difficulty and there was considerable bleeding The lesion extended over an area of 5 cm and the fibrosis involved the entire wall of the esophagus The diaphragm was opened from the esophageal hiatus outward through the central tendon, and the stomach was mobilized along the greater and lesser curvatures, ligating the left gastric and left gastroepiploic vessels, but leaving the spleen intact. The esophagus was cut across at the cardia approximately 6 cm. below the esophagogastric junction, and the cardia was closed. The stomach was sufficiently mobilized so that it could be easily drawn up into the left hemithorax. The esophagus was transected 2 cm. above the superior edge of the lesion and this segment was removed. Esophagogastrostomy was carried out, utilizing an inner layer of chromic 3-0 catgut and an outer layer of interrupted 3-0 silk sutures; the stoma of the esophagogastrostomy was placed well down on the lesser curvature, almost at the antrum of the stomach. Following completion of the esophagogastrostomy, the lesser curvature of the stomach was approximated to the left border of the esophagus with interrupted 3-0 silk sutures. Following this, circumferential esophagofundopexy was carried out in the manner described above. The imbricating sutures were extended along the lesser curvature to a point well below the stoma of the esophagogastrostomy. Following completion of this procedure the stomach was anchored to the hiatus of the diaphragm with interrupted 3-0 silk sutures, and the chest was closed in layers, following the placement of two No. 45 Pezzer catheters. The patient's postoperative course was unremarkable.

Follow-up roentgenographic and esophagographic examinations have shown the absence of esophagitis and the patient has gained 45 pounds in weight.

Comment: This case illustrates the devastating effect of long-standing, neglected peptic esophagitis associated with the sliding type of esophageal hiatus hernia. Here it was impossible by dilatation to achieve any lumen in the distal third of the esophagus because of the great density and extent of the stricture. In such a case, in order to re-establish a lumen, resection of the stricture must be carried out. In this particular case, submucosal resection of the stricture according to the technique of Allison was considered, but it was impossible to develop a reasonable cleavage plain preserving the muscularis of the esophagus. For this reason resection of the strictured area was carried out with the reconstructive procedure as stated above.

SUMMARY

1. Experimental investigations are reported from which the procedure of circumferential esophagofundopexy has been developed.
2. The application of this procedure to cases of brachyesophagus and peptic ulceration of the lower third of the esophagus are discussed and several illustrative cases are presented.

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Discussion

DR WILLIAM E NEVILLE, Cleveland, Ohio —At the moment, having spent 3 days here in Los Angeles, I feel more competent to discuss the symptoms of esophagitis rather than the surgical management of it

Two years ago, before this Association, my associate, George Clowes, and I had the opportunity to present our results in colon replacement of the esophagus The satisfactory results in patients operated on for carcinoma led us to extend this operative procedure to other conditions involving the esophagus

In order to evaluate whether it would be feasible to replace the lower end of the esophagus with the colon, we took the problem to the laboratory

[Slide] This is an autopsy specimen taken from a dog operated upon and sacrificed at the age of 9 months This is the esophagus, this is the transplanted colon segment and this is the stomach and, as you can all see, there is no evidence of esophagitis colitis or gastritis

At that time we thought this was a pretty severe test for the efficacy of this procedure, due to the fact that all of these dogs had marked regurgitation

[Slide] Commensurate with this, we began seeing patients who died as a result of progression of their disease up to 2 to 3 years following the operation for the resection of carcinoma This shows the esophagus which, as you can all see, is normal in appearance and this is the transplanted colon segment

[Slide] This is another patient who succumbed to the ravages of his disease This is a microscopic section, as you can all see, right at the esophagocolon anastomosis This shows normal appearing mucosa at the level of the esophagus, and this is, of course the colon transplant with no evidence of ulceration

[Slide] This patient was operated upon, having come in with a severe esophagitis with a recurrent hiatal hernia Repeated dilatations failed to alleviate the symptoms, and for this reason we resected the esophagus and interpolated a segment of transverse colon between the upper end of the esophagus and the stomach This man has been completely restored to normalcy as far as his esophagus is concerned

[Slide] This last slide shows a lesion in the lower end of the esophagus with stenosis for which resection was done and the colon interpolated between the esophagus and the stomach

We have only operated upon six patients to date for severe stenosing esophagitis, but it does seem to be a reasonable approach to the problem in the severe disabling form of this disease

DR J GORDON SCANNELL, Boston, Mass —I have enjoyed Dr Watkins' description of this most ingenious procedure very much, but I rather hope that in closing he will tell us how many cases, and how long these have held up

DR CAMERON HAIGHT, Ann Arbor, Mich —The procedure which Dr Watkins has illustrated has, I believe, a great deal to offer I am very much intrigued by it and I would particularly like to ask him if he has used it in conjunction with any colon transplant operations, because it would seem, a priori, that it might have a decided advantage in such cases

I would like to mention one physiologic disadvantage of a right colon transplant It offers no protection against regurgitation from the stomach into the transplanted colon This can be readily demonstrated by x ray *examination When barium has been intro*duced through the gastrostomy tube postoperatively with the patient in the upright position, the barium remains largely in the stomach However, when the patient is placed in the supine position, there is very extensive and prompt regurgitation of the barium into the transplant This is undesirable physiologically because it allows retention of feedings in the transplant when the patient is in the supine position and asleep It also allows air to come up freely into the transplant

Fortunately, however, with the colon there does not seem to have been acid irritation and ulceration of the transplant, as observed by examination of the stomach and adjacent colon with a cystoscope introduced through the gastrostomy.

We have used a right colon transplant in 3 adults who have had strictures of the lower esophagus either from peptic esophagitis or from caustic causes. Our reason for the choice of the colon for reconstruction of the esophagus was that all patients previously had extensive gastric resections because of the accompanying pyloric lesions. It was not believed possible to resect the extensive strictures of the esophagus in these cases and to bring the remaining small portion of the stomach high enough into the chest to perform an esophagogastrostomy. A right colon transplant would appear to be particularly useful in such patients who have previously had a very extensive subtotal gastric resection in conjunction with peptic esophagitis.

DR. F. HENRY ELLIS, JR., Rochester, Minn.—I would like to comment primarily on the theoretical basis of Dr. Watkins' interesting surgical procedure. I inferred from his presentation that he believes the esophagogastric angle is chiefly responsible for preventing regurgitation under normal conditions. Considerable controversy exists regarding the mechanism that prevents gastroesophageal regurgitation, but there is increasing evidence that the esophagogastric angle not only may not exist at all but, if it does, that it does not contribute to the prevention of reflux.

Physiologic studies give increasing evidence of the fact that there is a physiologic, if not an anatomic, esophageal sphincter that, together with some other factor such as a valve-flap mechanism at the cardia, may be of chief importance in preventing reflux.

Experimentally, Dr. Meiss in our laboratories has shown that the gastroesophageal angle can be completely obliterated provided the esophagogastric junction is not disturbed. Thus, our results were opposite to those Dr. Watkins has described in carrying out experimental fundusectomy. I would like to ask him more about the technique of his fundusectomy. I wonder if, in his experiments, he perhaps interfered in some way with the integrity of the esophagogastric junction in the process of excising the gastric fundus.

DR. WATKINS (Closing).—I would also like to emphasize that we are talking about a procedure which is applicable to a very small group of patients who represent the end and devastating result of peptic esophagitis which should have been treated much earlier by the methods which Dr. Cross emphasized previously.

I don't think from our experiments, whether they are animal or whether they are simple observations on postmortem specimens, that there is any doubt but that the angle furnishes some type of augmentation. Whether this is a mucosal flap or some other structure I can't say. I think it is a mucosal flap. This is augmented by having an acute angle between the esophagus and the stomach. It is easy to demonstrate this by applying water pressure through the pylorus into the stomach with the fundus of the stomach isolated from the body by a clamp or by augmenting it by excising the left leaf of the diaphragm.

The fundusectomies which were carried out here experimentally dividing the sling muscle as best we could do it technically.

We have not used colon transplants, in answer to Dr. Haight's question, in combination with this procedure. We have used left colon transplants to replace the esophagus, placing it substernally following total esophagectomy according to the technique of Orsoni.

I have used colon in this place because I have always thought the adequate mucous production by the colon offered more adequate protection against acid peptic digestion than did jejunum.

The observations of Dr. Ellis regarding a functional sphincter in the distal esophagus are most interesting. Dr. Lerch, who has been a member of this Society for many years, demonstrated to his satisfaction but not to that of all anatomists that such a structure does actually exist. We have not been able to demonstrate it.

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RESULTS

Seven experiments were discarded because of changes in the blood in the oxygenator which could have influenced the oxygen saturation. In the remaining 18 experiments, reduction in the pH was brought about in all cases. Correction of the reduced pH was accomplished in 11 experiments by the addition of sodium bicarbonate, by the creation of respiratory alkalosis in 2, and by the addition of molar sodium-r-lactate in 1. In 4 other animals, the addition of sodium lactate failed to bring about elevation in the pH.

TABLE I. EFFECT OF CORRECTED pH*

	INITIAL				OBSERVED				CALCULATED		
EXPER. NO.	ARTERIAL pH	pO_2 (MM. Hg)	ART. SAT. (%)	VEN. SAT. (%)	ARTERIAL pH	pO_2 (MM. Hg)	ART. SAT. (%)	VEN. SAT. (%)	ARTERIAL pH	pO_2 (MM. Hg)	ART. SAT. (%)
1	7.27	48	74.0	—	7.42	48	80.8	—	7.27	48	74
2	7.18	75	88.5	55.0	7.30	80	92.8	60.8	7.18	80	90
3	7.25	70	88.6	—	7.60	62	96.0	—	7.25	62	84
4	7.27	56	81.0	56.0	7.70	32	76.5	53.0	7.27	32	50
5	7.23	43	67.2	—	7.52	35	72.8	—	7.23	35	34
6	7.35	41	70.8	—	7.59	34	75.6	—	7.35	34	42
7	7.28	58	83.5	17.4	7.35	55	84.7	16.3	7.28	55	80
9	7.26	100	99.5	—	7.45	46	82.0	—	7.26	46	70
12	7.21	55	72.0	49.3	7.26	35	60.0	17.8	7.21	35	52
15	7.14	43	58.0	23.0	7.38	30	55.0	10.7	7.14	30	48
17	7.28	66	88.0	49.3	7.54	56	92.0	49.2	7.28	56	81
18	7.24	55	79.8	35.3	7.46	46	83.6	83.6	7.24	46	69
19	7.25	103	98.0	63.5	7.61	38	81.7	43.5	7.25	38	50
20	7.28	85	94.3	61.0	7.40	56	87.9	54.6	7.28	56	80
Averages	7.25	64	81.7	45.5	7.47	47	80.1	43.3	7.25	47	65

*This table depicts the degree of oxygen saturation of the blood which was obtained when the oxygen tension was reduced and the pH simultaneously elevated by the addition of alkali or the creation of respiratory alkalosis. The calculated results are theoretical saturations which would have been expected if the pH were not corrected as the oxygen tension was decreased.

Table I depicts the pH, partial pressure of oxygen, and the arterial and venous saturation before and after the correction of the pH. In Column 3 of Table I are the calculated oxygen saturations of the arterial samples which would have been present at the reduced PO_2,* if the pH had not been corrected. It is observed (Table I) that in the 14 experiments in which the pH was corrected that the observed average oxygen saturation was 15 per cent greater than the calculated arterial saturation despite the reduction in the oxygen saturation and partial pressure.

Table II shows the arteriovenous difference which was obtained in 9 of the experiments before and after the correction of the pH. It is noted that the elevation of the pH, although allowing the blood to pick up additional oxygen during its passage through the oxygenator, did not inhibit the release of this oxygen to the tissues since the arteriovenous difference is greater, despite the shift of the oxyhemoglobin dissociation curve toward the alkaline side. This apparent discrepancy in the action of the oxyhemoglobin dissociation curve is explained below.

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*Partial pressure of oxygen in millimeters of mercury.

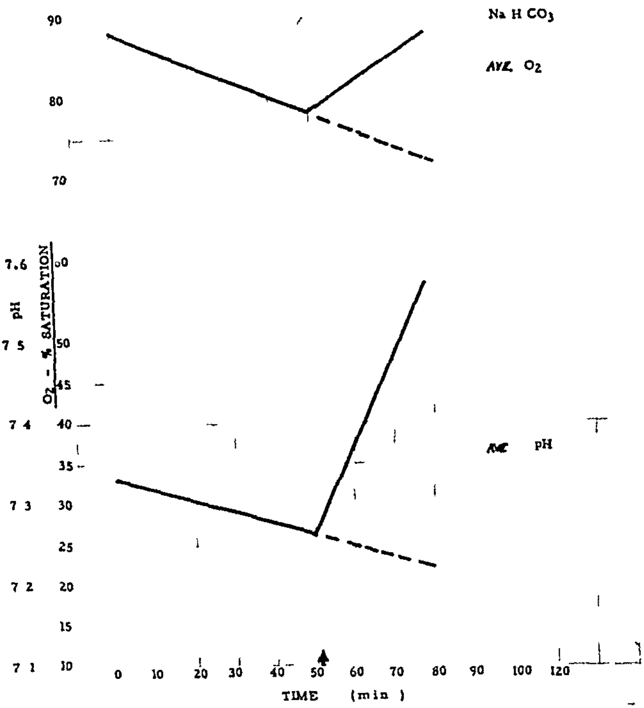

Fig. 2.—Curve showing the change in the average pH and oxygen saturation during the onset of hypoxia and after the addition of sodium bicarbonate.

TABLE II. ARTERIOVENOUS DIFFERENCE*

EXPER. NO.	LOW pH		HIGH pH	
	ART. SAT. (%)	VEN. SAT. (%)	ART. SAT. (%)	VEN. SAT. (%)
2	88.5	55.0	92.8	60.8
4	81.0	56.0	79.5	53.0
7	83.5	17.4	84.7	16.3
12	72.0	49.3	60.0	17.8
15	58.0	23.0	55.0	10.7
17	88.8	49.3	92.0	49.2
18	79.8	35.3	83.6	46.1
19	98.0	63.5	81.7	43.5
20	94.3	61.0	87.9	54.6
Averages	82.7	45.5	80.5	39.1
A-V Difference	37.2		41.4	

*The arteriovenous difference in 9 animals before and after the correction of the pH of the blood. This shows that the correction of the pH toward the normal or alkaline range did not prevent oxygen dissociation in the capillaries.

TABLE III. SODIUM BICARBONATE*

EXPER. NO.	LOW pH	ART. O_2 (%)	ART. CO_2 (VOL. %)	pCO_2 (MM. Hg)	$BHCO_3$ (mM/L.)	HIGH pH	ART. O_2 (%)	ART. CO_2 (VOL. %)	pCO_2 (MM. Hg)	$BHCO_3$ (mM/L.)	$NaHCO_3$ (mEq.)	TIME (DIF. MIN.)
1	7.27	74.0	—	—	—	7.42	80.8	—	—	—	133.8	63
2	7.00	85.5	40.5 (% Sat.)	—	—	7.30	95.8	85.1 (% Sat.)	—	—	624.4	55
3	7.25	88.6	29.9	33.8	14.4	7.60	96.0	65.5	37.0	35.0	156.1	20
4	7.25	70.4	—	—	—	7.70	79.5	—	—	—	156.1	75
5	7.23	67.2	—	—	—	7.52	72.8	—	—	—	89.2	25
6	7.20	68.8	—	—	—	7.59	75.6	—	—	—	111.5	25
7	7.28	83.5	8.4	7.2	4.25	7.78	86.3	34.0	13.5	19.4	89.2	30
9	7.17	95.1	38.9	51.7	17.9	7.45	82.2	75.1	58.5	39.3	133.8	35
15	7.14	88.7	43.8	66.0	22.0	7.38	55.5	40.2	36.7	20.8	44.6	9
19	7.25	97.4	36.0	50.8	17.2	7.61	98.2	54.7	46.5	27.6	44.6	19
20	7.13	90.8	28.9	43.3	14.1	7.40	87.9	45.3	40.3	24.1	44.6	17

*The results in eleven of the *experiments in* which sodium bicarbonate was used to *correct* the acidosis. The last two columns show the number of milliequivalents given and the time in minutes between the lowest and highest pH determinations.

Table III and Fig. 2 illustrate the changes in those animals which received sodium bicarbonate. The pCO_2 and $BHCO_3$ determined in 6 of these experiments shows that the addition in the total carbon dioxide content of the blood is reflected as an increase in the $BHCO_3$.

TABLE IV. SODIUM LACTATE*

EXPER. NO.	LOW pH	ART. O_2 (%)	HIGH pH	ART. O_2 (%)	TOTAL LACTATE (C.C.)	TIME (DIF. MIN.)	O_2 & CO_2 (%)
11	7.48	94.02	7.24	96.66	120	34	95 & 5
12	7.21	72.95	7.36	60.26	80	35	95 & 5
13	7.32	94.11	7.29	72.21	200	38	95 & 5
14	7.29	77.13	7.21	63.10	160	50	95 & 5
16	7.28	93.70	7.11	88.68	160	25	95 & 5

*The results in 5 animals given 1 M sodium-r-lactate solution. Note the failure to change the pH of the blood, and the continued fall in oxygen saturation. The time differential is the time between the addition of lactate and the taking of the sample for pH and oxygen saturation. Column 3 is labeled "high pH" and is the pH after the addition of sodium lactate. Note the failure to raise the pH in four of the five experiments.

Table IV depicts the results in those animals who received sodium lactate 150 to 200 c.c. of a molar solution. Four of the 5 animals failed to show any change in the pH of the blood. In 2 experiments, a change in the pH was induced by the development of respiratory alkalosis. This is illustrated in Table V and shows that respiratory alkalosis can induce a marked change in the pH. No striking change in the arteriovenous difference was noted so that the amount of oxygen delivered to the tissues was apparently not increased.

TABLE V. RESPIRATORY ALKALOSIS*

	pH	ART. O_2 SAT. (VOL. %)	ART. CO_2 (VOL. %)	ART. pCO_2 (MM. Hg)	ART. $BHCO_3$ (mM/L.)	VEN. O_2 (VOL. %)
Experiment 17						
95% O_2 and 5% CO_2	7.21	15.69	52.01	52.3	21.7	8.95
	7.28	15.20	55.94	51.0	23.5	—
100% O_2	7.49	15.24	46.45	33.0	19.5	8.22
	7.54	15.44	45.54	23.8	19.5	8.21
			Capacity 16.55			
Experiment 13						
95% O_2 and 5% CO_2	7.24	14.23	51.89	52.0	22.5	6.22
100% O_2	7.45	14.90	40.24	25.1	17.3	8.21
			Capacity 17.54			

*The effects of respiratory alkalosis produced in 2 animals by removing carbon dioxide from the oxygenating mixture. Note the marked reduction in pCO_2.

DISCUSSION

The design of the experiment was to reproduce the clinical situation resulting in inadequate oxygenation of the patient during cardiopulmonary bypass. This has been shown to result in a gradual production of metabolic acidosis.[4] Clinically this can occur if the flow rate of the patient exceeds the oxygenating capacity of the oxygenator or by the opposite situation of inadequate venous return because of insufficient gravity, faulty placement of the caval catheters.

or blood loss. This will result in inadequate arterial output and, despite adequate oxygenation of the blood as it passes through the oxygenator, the total amount of oxygen delivered to the patient will not supply his demand. The situation to a lesser degree may also be encountered if the donor blood is improperly stored and glycolysis markedly reduces the pH of the blood. This latter situation may be particularly compounded in those patients with cyanotic heart disease in whom it has been shown that some degree of metabolic acidosis is present.[9] These patients frequently, during preparation for bypass, will have a reduced cardiac output with hypotension and additional acidosis may occur before actual bypass is begun. Considerable desaturation of the tissues may be present and, if a high flow rate cannot be achieved to correct this during bypass, further acidosis and desaturation of the blood occurs, resulting in a markedly desaturated venous return which may overtax the efficiency of the oxygenator. The net result in these situations is a fall of oxygen tension, inadequate oxygen saturation, tissue hypoxia, and metabolic acidosis.

The body has two main lines of defense to prevent further hypoxia. They are the favorable dissociation of oxyhemoglobin at low oxygen tissue pressures and the reinforcement of this effect by the pH gradient between the arterial and capillary blood favoring further release. Because of the S-shaped curve of oxyhemoglobin dissociation it was necessary to illustrate these effects in our experiments to reduce the oxygen tension of the blood to approximately 30 to 50 mm. Hg. As is illustrated in Fig. 1, at higher oxygen saturations, changes in pH would not well illustrate the Bohr effect. As the disk speed was reduced, however, it was impossible to achieve a constant oxygen tension since the animal was continuously depleting the oxygen content of the arterial return and, during the time that the bicarbonate, lactate, or respiratory alkalosis was effected, further reduction in the tension took place. We, therefore, determined the oxygen tension at the pH and oxygen saturation of the arterial blood before and after the correction of the pH and calculated what the saturation of the arterial blood would have been at this reduced oxygen tension if the pH had not been corrected. This is shown in Table I. In those instances in which the arterial saturation was within normal range and in which oxygen tension was only mildly reduced when the pH was concomitantly reduced the addition of sodium bicarbonate actually raised the oxygen saturation, illustrating the true Bohr effect, that is, an increase in the oxygenation of the blood by the addition of alkali at a constant oxygen tension. In the remaining instances, although the correction of the pH did not raise the oxygen saturation of the blood, when compared to the initial sample, this could not be expected because of the continuing drop in oxygen tension. It did, however, prevent a further loss of saturation since, despite the further reduction in oxygen tension, an almost similar average arterial oxygen saturation was achieved. The fundamental question to be answered, however, was the method by which the arterialized blood achieved greater saturation. Was this at the expense of the tissues? Did the elevation of the pH in effect prevent release to the tissues so that the arteriovenous differences before and after the correction of the pH were essentially similar?

Table II shows the arteriovenous differences and, on the average, the tissues were able to extract more oxygen after the correction of the pH than before It will be noted that at the higher oxygen saturations the change in arteriovenous difference was insignificant despite the correction of the pH However, at the reduced saturations there were greater arteriovenous differences This can be explained from the dissociation curve At the higher saturations, pH has little effect on dissociation, but at reduced tensions it becomes quite significant For example, Fig 3 is a line chart showing the amount of oxygen bound by the hemoglobin of the blood of Dr A V Bock at varying oxygen tensions and serum pH At 30 mm of oxygen tension, increasing the pH from 7 25 to 7 70 increases oxygenation 35 per cent The converse of this is also illustrated in Fig 3 where the slight lowering of the blood pH when it receives carbon dioxide from the tissues assists in releasing additional oxygen Thus, from the above chart, it is evident that if Dr Bock at work had maintained an arterial pH in the capillaries, a drop to 32 mm of oxygen tension in the capillaries would have left 56 per cent of the venous hemoglobin in the oxygenated state instead of the observed 50 per cent This represents 13 per cent of the total oxygen released from the blood that is due to the slight lowering of the pH

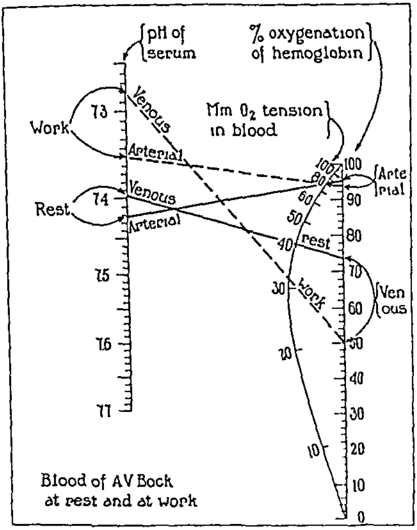

Fig 3 —*Line chart* showing the amounts of oxygen bound by hemoglobin of the blood of Dr A V Bock at different serum pH and oxygen tension (Ref 7)

The effect of oxygen tension in vivo is illustrated in Fig 1 At pH 7 4, the first 30 mm of oxygen tension grosses 56 per cent oxygenation of the hemoglobin in contrast to an increase of 30 mm of tension at the top of the scale changing the oxygenation only 6 per cent. When unusual demands in the tissue require oxygen, the last 30 mm. of oxygen tension causes a yield of more than half the arterial oxygen content. It is evident that at high oxygen tensions the addition of alkali to the blood will have little physiologic advantage but in situations as may occur during extracorporeal circulation in which the arterial saturation is reduced and tissue hypoxia is present, the correction of the pH toward the alkaline side will allow greater uptake of oxygen in the oxygenator, but will not affect the tissue pH to the extent that it will not be able to extract this additional oxygen from the blood as it reaches the tissue. We believe from our results that the correction of the pH allowed the blood to combine with more oxygen during its passage through the oxygenator increasing the total amount of oxygen available. However, on reaching the tissues the reduced oxygen tension and the additional tissue acidosis more than offset the increased oxygen affinity brought about by the change to the alkaline side, and therefore more oxygen was actually released to the tissues. In addition, by preventing further desaturation of the venous return additional strain on the oxygenator was prevented. The cycle of events which could be brought about by further venous desaturation, that is, reduced arterial saturation, reduced tissue oxygen tension, further extraction of oxygen, and a further reduction in venous saturation, was ameliorated.

One of the practices which is carried out during cardiac surgery is to hyperventilate the patient prior to bypass, creating a respiratory alkalosis and an elevated pH. This change in pH should favorably effect the oxyhemoglobin dissociation curve if severe hypoxia is present as illustrated above. However, recent work[10, 11, 12] has shown that hyperventilation is accompanied by increased production of lactic acid. This is predominantly an intracellular acidosis and is accompanied by an exchange of sodium for hydrogen ion. Elkinton and his co-workers[11] have shown that in acute respiratory acid-base disturbances transfer of intracellular cation occurs probably as the result of the changes of extracellular pH. No positive or negative load of fixed cation is imposed on the body as in the case of metabolic disturbances. Ninety per cent or more of the change in effective extracellular bicarbonate was extrarenal[10] and was related to changes in hydrogen ion uptake or release by buffer protein in the blood and by ionic transfer into or out of the cellular fluid in the body. Their results in respiratory alkalosis indicate that part of the cellular buffering consisted in release of hydrogen ion with the release of an undetermined ion, probably lactate, since an increase of extracellular lactic acid has been specifically reported to occur with respiratory alkalosis.[12, 13] Thus, it would appear that deliberate introduction of respiratory alkalosis before bypass would result in increased lactic acid formation and be actually more detrimental to the patient during extracorporeal circulation.

Table II illustrates the failure of sodium lactate to produce any change in the pH of the blood in 4 of the 5 animals when it was added during extracorporeal circulation. The lactate was administered rapidly and the animal received approximately 150 to 200 c.c. of molar sodium lactate in a half-hour period. Although the blood sodium following lactate administration became elevated, obviously sufficient time had not elapsed for the metabolism by the liver to release bicarbonate During extracorporeal circulation to effect changes in pH, sodium lactate is apparently not rapidly enough metabolized to effect these changes

With the present improvements in pump oxygenators and the greater experience gained from their application, oxygenation of blood does not now appear to be a significant problem However, occasionally situations do arise in which, because of blood loss or lack of blood reserve in the system, a compromise on the flow rate may become necessary Under these circumstances, increasing metabolic acidosis will result and the addition of sodium bicarbonate to counteract the release of lactic acid in this situation appears to be indicated During the past year we have continuously monitored pH of the blood during bypass and if the pH falls below 7 3 sodium bicarbonate, 4 mEq per kilogram of body weight is given directly into the oxygenator This has been given over a 10 minute period on 12 different patients and it has been noted in these cases to effect correction of the pH and at times a gross improvement in the oxygenation of the blood In these cases, we have not observed any adverse effects and found that postoperative acidosis, as illustrated by urine pH and blood pH determinations which would have been expected in these cases, has not been a problem

SUMMARY

Eighteen mongrel dogs were placed on extracorporeal bypass and metabolic acidosis was deliberately introduced by underoxygenation of the blood When the pH of the blood was lowered, blood samples were taken for arterial and venous oxygen saturations The pH was then corrected in 14 of these animals It was done by the addition of sodium bicarbonate in 11 with the creation of respiratory alkalosis in 2 and the addition of sodium lactate in 1, the addition of sodium lactate in 4 other animals failed to affect any change in the pH Oxygen tension was determined from the pH and the saturation of the blood at the corrected pH and compared to the calculated oxygen saturation of the blood at the same oxygen tension if the pH were not corrected The data illustrated that the Bohr effect, particularly at reduced oxygen tensions, raised the oxygen saturation of the blood during its passage through the oxygenator approximately 15 per cent Despite the correction of the pH, a greater arterial venous difference was noted, thereby effecting greater transport of oxygen to the tissues The effect of sodium lactate was found in 4 out of 5 animals to be ineffective in creating a pH change This is explained by the inadequate time elapsed between the addition of lactate and the pH determinations to allow for sufficient metabolism of the lactate Respiratory alkalosis was effective in 2 animals in elevating the pH and the physiologic effects of respiratory alkalosis were briefly discussed The clinical application of the results of this experiment was briefly presented

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(For Discussion, see page 638.)

STUDIES OF EDGLUGATE-Mg: A NEW DONOR BLOOD ANTICOAGULANT—PRESERVATIVE MIXTURE FOR EXTRACORPOREAL CIRCULATION

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The clinical application of extracorporeal circulation brought with it the need for relatively large amounts of heparinized blood freshly drawn from compatible donors. Already, the increasing use of this essential but sanguivorous adjunct to modern cardiovascular surgery is placing such a burden on some blood banks and donor programs as to interfere seriously with their efficient operation and their provision of blood for ordinary needs. In some localities, this "fresh blood" problem has been the major factor limiting both the frequency and convenient scheduling of open heart operations. When, after the donor blood is drawn, such operations are canceled, or the intended extracorporeal circulation not employed, blood banks have on short notice the unhappy choice of quickly finding other suitable recipients for this group specific blood of short storage life or of discarding it altogether as waste. In such cases, the expedient of re-entering the blood container to add a second anticoagulant—preservative solution such as acid-citrate-dextrose (ACD) is unacceptable because of the potential hazard of bacterial contamination.

The design of an ideal donor blood anticoagulant—preservative mixture for use in extracorporeal circulation should consider the desires of the following:

Blood banks would like (1) to accumulate donor bloods 1 to 5 days preoperatively; (2) to use conventional, inexpensive donor equipment; and (3) if the blood is not used for extracorporeal circulation (a) to avoid re-entry of container with anticoagulant—preservative mixture and (b) to use for routine transfusions up to 2 to 3 weeks of storage.

The surgeon would like (1) relatively fresh blood with (a) good osmotic and mechanical resistance, (b) maximal red blood cell viability, (c) intact coagulation components; (2) anticoagulant—preservative mixture permitting (a) minimal dilution of blood, (b) compatible plasma electrolyte pattern, (c) no clots or fibrin, (d) near normal pH (at 37° C.); (3) to have blood on hand at all times for emergency perfusions.

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Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles, Calif., April [illegible], 1959.

The patient's family would like to avoid the cost of professional donors.

Blood donors would like to donate blood at their convenience during the 5 days before operation.

In the hope of fulfilling most of these desires, we began studies of various anticoagulant—preservative mixtures about 2 years ago. These studies included certain exchange resins and sequestering agents combined with sugars and stabilizing salt solutions. Of the numerous combinations studied thus far, only a mixture of disodium ethylenediamine tetraacetic acid, glucose, sodium gluconate, and magnesium chloride has shown sufficient promise to warrant clinical trial. This report describes a portion of our most significant studies of this anticoagulant—preservative mixture and records our clinical experience employing it for donor blood during the past few months.

MATERIALS AND METHODS

The composition of Edglugate-Mg,* the solution finally adopted and upon which these studies are based, is given below.

$Na_2H_2EDTA\cdot 2H_2O$	0.41 Gm.
Sodium gluconate (anhyd.)	0.364 Gm.
Dextrose (anhyd.) USP	1.50 Gm.
$MgCl_2\cdot 6H_2O$	0.305 Gm.
Water q.s. ad	30.0 ml.

The above mixture in a volume of 30 c.c. was prepared and sterilized in plastic bag containers.

After venipuncture, 500 c.c. (530 Gm.) of whole blood were drawn into each bag by gravity with frequent agitation to ensure complete mixing. Care was taken not to overfill any of the bags. The bags of blood were then stored in a blood bank refrigerator at 2° to 6° C. until shortly before use.

Conversion for Priming Blood in Extracorporeal Circulation.—Only bags of blood which had been stored *for 5 days or less* were used in priming the heart-lung machine and filling the extracorporeal reservoir. For this use, each bag was first "converted" (Fig. 1) by adding 15 mg. (1,500 units) of commercial heparin by syringe and needle through the rubber bung of the bag closure. After thorough mixing, 5 c.c. of a sterile aqueous solution of calcium chloride containing 1.67 mM of Ca^{++} (0.2425 Gm. calcium chloride USP) was added to each bag in order to restore the ionized calcium to slightly above the normal blood level. After mixing thoroughly by tilting the bag, the blood was introduced into the extracorporeal apparatus or reservoir. In most instances the "conversion" of these donor blood units was carried out within 15 to 30 minutes of the start of the perfusion.

Bags of blood not used for extrocorporeal circulation, but employed for routine transfusions, were stored for various intervals up to 21 days before administration. For this purpose no "conversion" or additives were employed, the blood being administered as any ordinary transfusions directly after removal from the blood bank. In many instances, samples of blood were taken aseptically from each bag just before use for the various determinations listed below. A large number of bags of blood were drawn from donors and stored for study purposes only. Sterile samples were drawn from these bags for various studies at regular intervals throughout the refrigerated storage period. Because of the multiple re-entries into these bags with the potential danger of contamination, they were not considered suitable for transfusion purposes.

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*This solution was prepared and supplied to us in sterile plastic containers by the Cutter Laboratories, Berkeley, Calif.

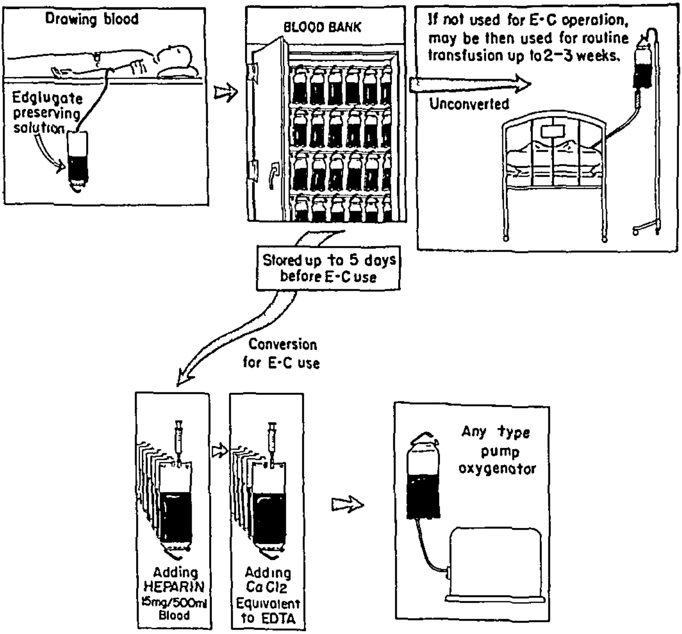
Drawing blood
Edglugate preserving solution
BLOOD BANK
If not used for E-C operation, may be then used for routine transfusion up to 2–3 weeks.
Unconverted
Stored up to 5 days before E-C use
Conversion for E-C use
Adding HEPARIN 15mg/500ml Blood
Adding CaCl2 Equivalent to EDTA
Any type pump oxygenator

Fig 1—Picture diagram of collection, storage, and alternative uses of Edglugate blood. The amount of blood being collected is measured by a carefully calibrated spring scale. During drawing the plastic bag and its contents are frequently agitated and kneaded to ensure swift thorough mixing of blood with anticoagulant. For conversion we have found that 15 mg (1,500 units) of heparin and 1.65 mM $CaCl_2$ per 500 c.c. unit of blood are satisfactory. This amount of $CaCl_2$ is 50 per cent excess over theoretical to offset the physiologic effect of the elevated plasma K^+ level of the blood. Filtering the blood while priming the pump-oxygenator may be advisable depending upon the design of the equipment and the adequacy of the blood drawing technique.

Clinical perfusion equipment and techniques used in our hospital have been described previously.[1] Hypothermia produced by a blood heat exchanger[2] was employed in all cases and each patient was on partial perfusion for 3 to 10 minutes during the cooling phase before total bypass was begun. Flow rates averaged 50 c.c. per kilo per minute for patients weighing 35 Kg. or less and 30 c.c. per kilo per minute for patients weighing over 35 Kg. Duration of perfusions ranged from 15 minutes to 1 hour and 20 minutes.

Laboratory determinations of whole blood pH, blood oxygen content,[3] blood CO_2 content, blood buffer base,[4] sodium and potassium, plasma hemoglobin, erythrocyte osmotic fragilities, partial thromboplastin times,[5] blood clotting times, recalcification clotting times, fibrinolysin activity, plasma fibrinogen,[6] and plasma factor V assay[6] were made by the methods referred to or by other standard procedures. Antihemophilic globulin (AHG) assays were carried out by the partial thromboplastin time method of Langdell,[7] employing plasma from a known severe hemophilic patient with an AHG level of less than 1 per cent.

Determinations of in vivo red cell survival after various intervals of blood storage at 2° to 6° C. were made by autotransfusions in healthy volunteer subjects. The red cells in these survival experiments were tagged with Cr^{51} by the method of Read.[8] The initial red cell volumes of these recipients were determined by tagging separate aliquots of their own fresh red cells with P^{32}.

RESULTS

In Vitro Studies.—The results of in vitro studies of Edglugate blood after various intervals of storage at 2° to 6° C. are given in Table I. The most significant changes noted were an increase in plasma potassium levels, a prolongation of the partial thromboplastin time, and a decrease in the level of accelerator globulin (Factor V). The plasma potassium level was seen to rise to a plateau of around 25 mEq./L. after about 5 days of storage.

TABLE I. CHANGES OCCURRING IN EDGLUGATE-Mg BLOOD DURING STORAGE AT 2° TO 6° C.

DAYS STORAGE AT 2°-6° C.	pH 37° (MEDIAN)	K (mEq./L.)	Na (mEq./L.)	PTT (SEC.)	AHG LEVEL (%)	FACTOR V (%)	RECAL. CLOT. TIME (MIN./SEC.)	PLATELETS (THOUS./MM.³)	FIBRINOGEN (MG./100 ML.)	PLASMA Hb (MG./100 ML.)
0	7.17	6.2	141	(73)	89	(100)	3/30	258		2*
1	7.12	10.1	141				3/46	173		
2	7.08	15.0	141	181	49	18	3/51	213		
3	7.06	18.5	141	168			3/46	206		6†
4	7.03	19.9	141	129	20	6.1	4/21	226		
5	6.99	24.5	142	130	15	9.7	4/03		340	2*
6-10	7.0	27	131	144		9.7			301	12†
11-15	7.1	29	127	240		9.7			308	3*
16-20	7.2	27	132	357		0.7			292	

Each value in this table represents the average (or median) value obtained from studies of at least 10 pints of Edglugate donor blood. Some values represent studies on more than 600 pint units.

Average values in parentheses were obtained from citrated blood samples drawn from donors just prior to their 500 c.c. donations into the Edglugate-Mg bags.

*Average values of bags not agitated prior to sampling.

†Average values of same bags thoroughly mixed before each sampling.

Antihemophilic globulin levels were assayed on a group of Edglugate donor bloods after 2, 4, and 5 days of storage. There was a slight fall immediately after drawing the blood with a progressive decline to about 15 per cent of normal by the fifth day of storage.

The level of Factor V (accelerator globulin) also declined with storage, falling to about 10 per cent at the end of 5 days. There was some gradual increase in the recalcification clotting times during the first 5 days Platelet counts remained remarkably stable during this time, but with some variation in counts on individual bags Fibrinogen levels even at 20 days showed only an insignificant change Plasma hemoglobin levels did not show any significant increase during the storage period unless the bags were repeatedly mixed and allowed to resettle Under these circumstances there was a slight increase in plasma hemoglobin level that averaged less than 12 mg per cent after 6 to 10 days of storage Whole blood pH determinations made at 37° C remained relatively constant during the entire 20 day storage period in the range of 7 0 to 7 2

The results of in vivo red cell survival studies of Edglugate blood compared with blood stored in standard acid citrate dextrose after varying storage periods up to 21 days are represented by the curves in Fig 2

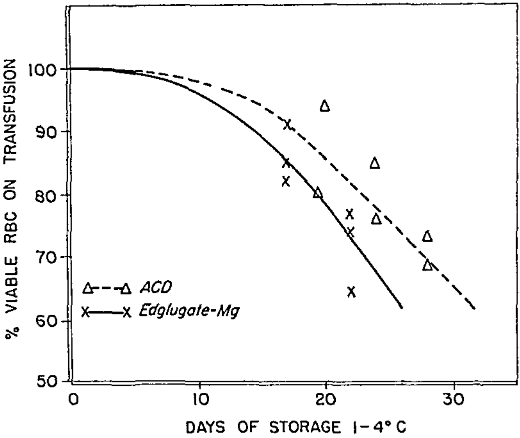

Fig 2—The in vivo viability of autotransfused erythrocytes of blood stored in Edglugate solution (*solid curve*) A curve of ACD blood erythrocyte survival (*broken line*) is included for comparison Edglugate blood has an erythrocyte viability of 73 per cent after 21 to 22 days of storage

It will be noted that there was no significant difference in red cell viability between bloods in these two anticoagulants during the first week of storage, both solutions providing better than 95 per cent survival At the end of 21 days' storage, Edglugate bloods showed survivals averaging approximately 72 per cent viable red cells whereas ACD bloods of the same age showed a slightly better viability with 78 per cent of the transfused cells surviving normally

Clinical Studies—Table II summarizes certain data on the 81 patients undergoing clinical perfusions in which Eglugate Mg donor blood from 1 to 5 days old was used exclusively for priming the heart lung machine and reservoir Here the volumes of Edglugate blood collected have been expressed in

TABLE II. EXTRACORPOREAL CIRCULATION PATIENTS PRIMING VOLUME EDGLUGATE-Mg BLOOD PER KILOGRAM BODY WEIGHT

VOLUME EDGLUGATE BLOOD	75 C.C./KG.	75-150 C.C./KG.	150-225 C.C./KG.	225-300 C.C./KG.	300 C.C./KG.
Body wt. range Kg.	45-97	22-59	15-27	12-16	3-12
No. patients	37	19	12	6	7
No. deaths	8	3	1	2	5
Platelet counts					
% of control*	35	43	48	34	34
Serum K					
% of control†	91	101	103	112	125

*Average platelet counts approximately 15 minutes postperfusion expressed as per cent of patient's pre-perfusion platelet count.

†Average serum potassium levels immediately postperfusion expressed as per cent of patient's pre-perfusion serum potassium level.

terms of the patients' weights in order to make better comparison of the donor blood priming volumes with the patients' original blood volumes. The number of patients in each volume-weight range is shown with the number of deaths in each group. Most of the deaths, 14 out of 19, occurred at the extreme ranges of donor priming volume to patients' weights. The number of patients and deaths are tabulated according to diagnosis in Table III. Most of the deaths in this series occurred among the patients with the most complicated and serious lesions. The average decrease in platelet counts postperfusion ranged between 52 and 66 per cent of the pre-perfusion counts for all the groups of patients.

TABLE III. OPERATIONS WITH EXTRACORPOREAL CIRCULATION EMPLOYING EDGLUGATE PRIMING BLOOD 1 TO 5 DAYS OLD

DIAGNOSIS	NO. PATIENTS	POST-OPERATIVE BLEEDING	DEATHS
Open-Heart Cases			
Atrial septal defects	18	0	0
Ventricular septal defects	10	1	3
Tetralogy of Fallot	13	0	2
Mitral stenosis or insufficiency	15	0	4
Pulmonic or aortic stenosis	13	0	2
Tricuspid atresia	1	0	1
Complete transposition	2	0	2
Total anomalous pulmonary venous drainage	2	0	1
Totals	74	1	15
Miscellaneous Perfusions			
Thoracic and ventricular aneurysms	4	0	3
Cerebral aneurysms and tumors	3	0	1
Totals	7	0	4

There was only a slight rise in the average postperfusion serum potassium levels, reaching 25 per cent or approximately 1 mEq./L. more than the pre-perfusion level in only the smallest patients in whom the volume of priming blood exceeded the patient's blood volume fourfold or more. When the priming donor blood had the highest plasma K levels and particularly when the patients were small with a high ratio of donor priming blood to patient's weight, a rise in the patient's serum K^+ level was occasionally seen a minute or so after starting the perfusion (Fig. 3). This rise in K rarely persisted more than 2 to 4 minutes and quickly fell and remained at normal levels during the remainder of the perfusion.

Changes in various blood coagulation components in 5 patients following perfusion with Edglugate blood are shown in Table IV

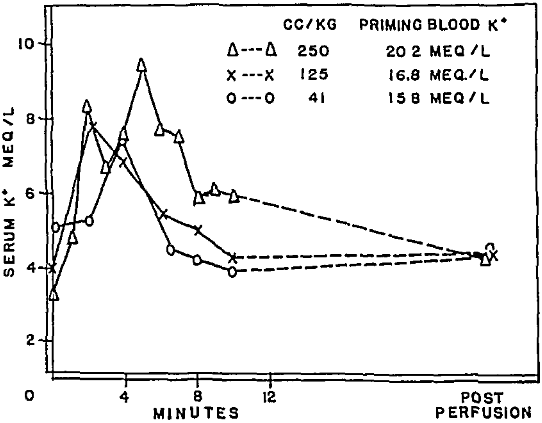

Fig 3 —Graph showing the change with time of the plasma K^+ levels in the venous return blood of 3 patients immediately after the start of extracorporeal perfusion with stored Edglugate blood Volumes of pump priming blood per kilogram of patient body weight and the plasma K^+ level of the blood at the start of perfusion are tabulated in the upper right (see text)

TABLE IV. COAGULATION CHANGES IN PATIENTS PERFUSED WITH EDGLUGATE Mg BLOOD

PT.	WT KG.	E G G BLOOD (C C)	AVG AGE (DAYS)	DURATION ECC (MIN.)	PLATELETS (THOUS / MM ³)	COAG TIME (MIN.)	AHG (%)	FACTOR V	LYSIN
A	32	4,000	2	39					
Pre perfusion					435	7	100	100	0
Postperfusion					173	7	100	55	0
B	21 3	4,000	2	69					
Pre perfusion					223	5	100	100	0
Postperfusion					193	9	48	49	0
C	12 3	3,500	3	54					
Pre perfusion					303	6	100	100	0
Postperfusion					223	14	42	17	0
D	12 3	4,000	3	46					
Pre perfusion					428	5	100	100	0
Postperfusion					153	12	1	30	+++
E	14 8	4,000	2	59					
Pre perfusion					395	6	100	100	0
Postperfusion					75	4	14	35	0

The distribution as to single, multiple spaced, and large simultaneous transfusions totaling 945 units of blood administered throughout the hospital as ordinary transfusions without "conversion" is listed in Table V.

TABLE V. DISTRIBUTION OF EDGLUGATE-Mg BLOOD AS ORDINARY TRANSFUSIONS GIVEN AS SINGLE AND SPACED OR LARGE TRANSFUSIONS (WITHIN 24-HOUR PERIOD) AFTER STORAGE AT 2°-6° C. UP TO 21 DAYS

	PINTS TRANSFUSED				
	1	2-4	5-8	9-12	12+
Patients receiving single or spaced transfusions	274	107	18	4	3
Patients receiving large transfusions	—	115	12	3	1
Total pints transfused—945					

DISCUSSION

While heparin is the only in vivo anticoagulant which has been found suitable for extracorporeal perfusion use, it is a poor anticoagulant for preserving donor blood for any length of time. Blood collected in heparin slowly escapes the anticoagulant effect and within 12 to 30 hours of storage usually becomes unfit for perfusion use.

Proper storage of donor blood for more than a few days requires more than the simple prevention of coagulation. Various substances must be added and physical conditions adjusted to minimize deterioration of both cellular and protein elements during storage. For example, without added glucose, erythrocytes soon lose viability which may not be signaled by hemolysis or changes in osmotic or mechanical fragility. When such red cells are returned to the circulation they are rapidly destroyed.

Certain coagulation components, particularly Factor V and AHG, disappear fairly rapidly from stored blood, and especially so if incipient clotting is started by faulty collection. No satisfactory way has yet been devised to extend the naturally short life spans of leukocytes and platelets in vivo or in vitro. These formed elements may appear morphologically normal in stored blood and yet be nonfunctional and nonviable after transfusion. Thus good platelet counts are probably meaningless on blood stored beyond 36 to 48 hours.[9]

Successful storage of whole blood for perfusion purposes depends upon devising a solution which preserves as far as possible the coagulation components, the erythrocytes and, within the limits of their natural life span, the blood platelets. The anticoagulant isotonicity, pH, dilution, and the presence or absence of various substances all affect the storage characteristics of different components of blood drawn into the mixtures.

Edglugate-Mg solution was devised as an anticoagulant—preservative mixture for donor blood which might be suitable for extracorporeal perfusion use up to 5 days' storage and ordinary transfusion use up to 21 days' storage. Sprague and his associates[10] showed that a mixture of EDTA (ethylenediamine tetraacetic acid) and glucose was a suitable anticoagulant preservative solution, at least with respect to red cell viability. EDTA has been used clinically as an anticoagulant for blood transfusions for some time, particularly for transfusions where platelet rich blood is desirable.

The disodium calcium salt of EDTA (the compound resulting on its addition to blood) has a very low toxicity in man. Administered as a chelating agent for toxic polyvalent cations, it has been used extensively for lead poisoning in children and for accidental ingestion of various radioisotopes. The only significant toxic effect reported thus far has been renal tubular damage after its prolonged use for lead intoxication.[11] None of this compound is metabolized and it is rapidly excreted by the kidney.

Disodium EDTA is a powerful sequestering agent of divalent cations and on a molar basis is five times as efficient as sodium citrate as an anticoagulant of blood.

Initial studies were made to find the least amount of EDTA which could be relied on to prevent even traces of coagulation in donor blood drawn by routine blood bank procedure. These studies revealed that the EDTA-Ca^{++} binding is not complete at normal blood pH and that a slight excess of EDTA is required above the stoichiometric quantity of calcium. We have found 1.1 mM of disodium EDTA to be a satisfactory amount for anticoagulating 500 c.c. of blood.

There is a sharp chemical equivalence relationship between Ca^{++} and the EDTA which permits the ionized calcium in blood anticoagulated with a minimum of EDTA to be restored rather precisely with a predictable minimum amount of a calcium salt. Actually, 1.1 mM of Ca^{++} results in a restoration of the blood ionized calcium level to a normal value in the presence of the inert calcium disodium EDTA complex. However, in the conversion of Edglugate blood for perfusion purposes we have chosen to add 1.65 mM Ca^{++} in view of the increased potassium content of the plasma which develops during the permissible storage period.

In our conversion of Edglugate blood for perfusion, we have added 15 mg. (1,500 units) of heparin just prior to the addition of the calcium chloride solution.

This principle of "conversion" of Edglugate-Mg blood with heparin and calcium ion raises the question of the feasibility of "converting" standard ACD blood for extracorporeal perfusion. Even though we are aware that this has been done by some heart surgical teams in desperate situations of large unexpected blood loss, ordinary ACD blood has certain characteristics which seriously detract from using it as the only source of priming blood. This blood is more dilute and carries with it a considerable burden of added sodium ion. In addition, it has a pH at body temperature which may be unacceptably low for extracorporeal perfusion during heart-lung bypass. Considerable citrate in excess of blood calcium must be present in ACD solution to force sufficient sequestration of Ca^{++} to prevent the blood from clotting. Even if the dilution and sodium burden were to be considered acceptable, the successful "conversion" would require the addition of a large and uncertain amount of calcium ion to the blood to equilibrate with the excess citrate, and some acceptable organic or mineral base should be added to adjust the pH.

In order that Edglugate blood might be preserved in storage for ordinary transfusions, should it not be used for extracorporeal circulation, glucose was added to the mixture. It has been shown previously[10] that the combination of

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EDTA and glucose gives satisfactory survival of red blood cells after storage up to 21 days. However, whereas we also found this combination to give good in vivo survival (see Fig. 2), we noted an increase in hemolysis and plasma hemoglobin between the second and third weeks of storage. We found this mild spontaneous hemolysis could be largely prevented by the addition of a small amount (1.67 mM) of sodium gluconate to the anticoagulant mixture.

The leakage of potassium ion from red cells to the plasma during the refrigerated storage of whole blood seems to be an unavoidable phenomenon which is influenced by the nature of the anticoagulant—preservative employed only in rate. Red blood cells stored in Edglugate lose potassium at a rate about double that of ACD blood. From the standpoint of its use in perfusions, this is perhaps the most important defect of this mixture.

We are hopeful that further adjustments of this anticoagulant—preservative still under study may decrease this rate of potassium loss with storage. Perhaps chelating the additional plasma potassium and any ammonia accumulated during storage on exchange resins at the time of transferring the blood into the heart-lung machine might be a practical solution, but thus far we have had no experience with this interesting technique recently suggested by Schechter.[12]

As illustrated in Fig. 3, a transient rise of plasma potassium occurs in some patients perfused with Edglugate blood within 2 to 3 minutes after starting perfusion. There is a simple correlation between the level reached and the potassium content (related to the age of the blood), volume of priming blood, and body weight of the patient. This additional plasma potassium is quickly taken up by the patient's relatively large intracellular space and the plasma potassium returns to normal in the next 2 to 4 minutes of perfusion.

As would be expected, the pH of Edglugate blood declines slightly during storage as the erythrocytes metabolize glucose and liberate free organic acids to the plasma. However, this fixed metabolic acid load contributed by Edglugate blood stored up to 5 days is of little consequence as indicated in a previous report from this laboratory.[13] During these studies of blood buffer base levels both during and following clinical perfusions, we found no significant differences between the series of patients perfused with fresh heparinized blood and the series perfused with stored Edglugate blood. In both groups of patients the decreases in blood buffer base were no greater than have been reported as resulting from nonperfusion thoracic procedures and anesthesia.[14]

Changes in certain coagulation components occurring in Edglugate blood during the first few days of storage are of particular interest.

Previously, it has been observed that disodium EDTA, particularly in excess, causes a rapid loss of plasma antihemophilic globulin and Factor V (accelerator globulin) activity.[15] More recently, Zucker and Borrelli[16] and Mustard[17] have shown that this effect of EDTA is decreased if the EDTA is kept to the minimum necessary for anticoagulation. Zucker and Borelli also found that the addition of magnesium inhibited the depression of the Factor V level. Thus besides keeping the disodium EDTA to the minimum levels mentioned previously, we have also included a small quantity (0.15 mM) of magnesium chloride in the Edglugate mixture. Despite this addition of magnesium ion, fairly rapid inactivation of both Factor V and antihemophilic globulin occurs during the first few days of storage (Table I). These changes are more rapid than those seen in citrated blood and probably represent a price which must be paid for the use of a potent chelating anticoagulant.

Didisheim[18] has reported that all other known coagulation components are relatively unaffected by EDTA. Despite this depression of antihemophilic and Factor V activity in stored Edglugate blood, we have encountered bleeding following extracorporeal circulation in only 1 patient. While in extremis, this woman developed a potent fibrinolysin after 2½ hours of pumping during a futile effort to sustain her failing heart.

In many of our patients having open heart operations, we have carried out extensive coagulation studies both pre- and postperfusion. Pertinent data from some of these patients are given in Table IV. It will be noted that in most of these patients there was a depression of AHG and Factor V levels postperfusion. None of these patients showed any evidence of postoperative bleeding.

One patient (D) had a 99 per cent reduction in the AHG level. However, the facts that the postperfusion clotting time was normal and that he showed no bleeding tendency would indicate that the moderate fibrinolysin also found in this patient might have accounted for the falsely low AHG assay.

It is of further interest that Hoeksema, Mustard, and Mustard[19] have recently reported similar depressions in AHG levels of 10 to 80 per cent following extracorporeal circulation in patients perfused with fresh heparinized blood. This would indicate, perhaps, that like the postperfusion depression of the platelet count, the depression of AHG level is more closely related to the duration of the perfusion and any in vivo activation of the coagulation process than to the AHG content of the priming donor blood. Recently, we have had the opportunity to test the in vivo effectiveness of Edglugate plasma in a hemophiliac (AHG deficient) admitted to the hospital for elective tooth extraction. The patient's trait was severe and two siblings and two cousins had died as a direct result of their disease. This patient's AHG level was corrected and maintained with Edglugate plasma, some of which had been stored at 2° to 6° C. for periods up to 5 days. Volumes of 200 to 400 c.c. of Edglugate plasma a day were completely adequate to control this man's bleeding tendency as measured by the PTT test[5] and allow the uncomplicated extraction of 6 teeth.

As mentioned above, morphologic maintenance of formed blood elements is not equivalent to viability. The platelet counts shown in Table I are quite respectable. Platelets in Edglugate-Mg blood are in the sphere form and remain intact without clumping for many days. However, from the studies of Krevans and Jackson,[9] it is very unlikely that these platelets are hemostatically functional in vivo after more than 1 or at most 2 days' storage. In spite of this, we have seen no purpuric manifestations in any of our patients or any bleeding attributable to thrombopenia. (Tables II, IV.)

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We are hopeful that further adjustments of this anticoagulant—preservative still under study may decrease this rate of potassium loss with storage. Perhaps chelating the additional plasma potassium and any ammonia accumulated during storage on exchange resins at the time of transferring the blood into the heart-lung machine might be a practical solution, but thus far we have had no experience with this interesting technique recently suggested by Schechter.[12]

As illustrated in Fig. 3, a transient rise of plasma potassium occurs in some patients perfused with Edglugate blood within 2 to 3 minutes after starting perfusion. There is a simple correlation between the level reached and the potassium content (related to the age of the blood), volume of priming blood, and body weight of the patient. This additional plasma potassium is quickly taken up by the patient's relatively large intracellular space and the plasma potassium returns to normal in the next 2 to 4 minutes of perfusion.

As would be expected, the pH of Edglugate blood declines slightly during storage as the erythrocytes metabolize glucose and liberate free organic acids to the plasma. However, this fixed metabolic acid load contributed by Edglugate blood stored up to 5 days is of little consequence as indicated in a previous report from this laboratory.[13] During these studies of blood buffer base levels both during and following clinical perfusions, we found no significant differences between the series of patients perfused with fresh heparinized blood and the series perfused with stored Edglugate blood. In both groups of patients the decreases in blood buffer base were no greater than have been reported as resulting from nonperfusion thoracic procedures and anesthesia.[14]

Changes in certain coagulation components occurring in Edglugate blood during the first few days of storage are of particular interest.

Previously, it has been observed that disodium EDTA, particularly in excess, causes a rapid loss of plasma antihemophilic globulin and Factor V (accelerator globulin) activity.[15] More recently, Zucker and Borrelli[16] and Mustard[17] have shown that this effect of EDTA is decreased if the EDTA is kept to the minimum necessary for anticoagulation. Zucker and Borelli also found that the addition of magnesium inhibited the depression of the Factor V level. Thus besides keeping the disodium EDTA to the minimum levels mentioned previously, we have also included a small quantity (0.15 mM) of magnesium chloride in the Edglugate mixture. Despite this addition of magnesium ion, fairly rapid inactivation of both Factor V and antihemophilic globulin occurs during the first few days of storage (Table I). These changes are more rapid than those seen in citrated blood and probably represent a price which must be paid for the use of a potent chelating anticoagulant.

Didisheim[15] has reported that all other known coagulation components are relatively unaffected by EDTA. Despite this depression of antihemophilic and Factor V activity in stored Edglugate blood, we have encountered bleeding following extracorporeal circulation in only 1 patient. While in extremis, this woman developed a potent fibrinolysin after 2½ hours of pumping during a futile effort to sustain her failing heart.

In many of our patients having open heart operations, we have carried out extensive coagulation studies both pre- and postperfusion. Pertinent data from some of these patients are given in Table IV. It will be noted that in most of these patients there was a depression of AHG and Factor V levels postperfusion. None of these patients showed any evidence of postoperative bleeding.

One patient (D) had a 99 per cent reduction in the AHG level. However, the facts that the postperfusion clotting time was normal and that he showed no bleeding tendency would indicate that the moderate fibrinolysin also found in this patient might have accounted for the falsely low AHG assay.

It is of further interest that Hoeksema, Mustard, and Mustard[19] have recently reported similar depressions in AHG levels of 10 to 80 per cent following extracorporeal circulation in patients perfused with fresh heparinized blood. This would indicate, perhaps, that like the postperfusion depression of the platelet count, the depression of AHG level is more closely related to the duration of the perfusion and any in vivo activation of the coagulation process than to the AHG content of the priming donor blood. Recently, we have had the opportunity to test the in vivo effectiveness of Edglugate plasma in a hemophiliac (AHG deficient) admitted to the hospital for elective tooth extraction. The patient's trait was severe and two siblings and two cousins had died as a direct result of their disease. This patient's AHG level was corrected and maintained with Edglugate plasma, some of which had been stored at 2° to 6° C. for periods up to 5 days. Volumes of 200 to 400 c.c. of Edglugate plasma a day were completely adequate to control this man's bleeding tendency as measured by the PTT test[5] and allow the uncomplicated extraction of 6 teeth.

As mentioned above, morphologic main[illegible] formed blood elements is not equivalent to viability. The platelet counts shown in Table I are quite respectable. Platelets in Edglugate-Mg blood [illegible] the sphere form and remain intact without clumping for many da[illegible], from the studies of Krevans and Jackson,[9] it is very unlikely that [illegible] are hemostatically functional in vivo after more than 1 or at most 2 [illegible] storage. In spite of this, we have seen no purpuric manifestations in any of our patients or any bleeding attributable to thrombopenia. (Tables I [illegible] IV.)

All of the patients reported in this study have been perfused by the hypothermic techniques in use at this center.[1] Because of the advantages which we feel to accrue from the combination of hypothermia and low-flow extracorporeal perfusion, we have not been willing to change our technique in order to study Edglugate blood under normothermic high-flow perfusion conditions. It is hoped that other groups evaluating this anticoagulant—preservative mixture will soon have sufficient data and experience to permit more full evaluation.

Table V summarizes the distribution of Edglugate-Mg blood for ordinary transfusion to patients on various services throughout the hospital over a 2-year period. A number of these units were distributed by the blood bank for ordinary transfusions after the heart operations for which they had been intended originally were delayed or cancelled for one reason or another. The remainder were collected during a period of 1 month when all donor blood collected in the Duke Hospital Blood Bank for all purposes was drawn into Edglugate-Mg solution. Aside from the small amount of citrated blood which was shipped to the blood bank from outside sources, every unit of blood given in Duke Hospital during this period of time was stored Edglugate-Mg blood handled through our ordinary transfusion procedures. No untoward clinical results were reported and the incidence of transfusion reactions was as low as or lower than our reaction rate with citrated blood. This portion of the study was conducted to assess the effectiveness of Edglugate blood for ordinary transfusions as compared with citrate blood. As noted in Table V, many patients received multiple spaced transfusions of this blood. Many others received large simultaneous transfusions with adequate response and without any discernible ill effects. The 945 units of Edglugate blood administered as ordinary transfusion added to the more than 600 units used in extracorporeal perfusion represents a total series in excess of 1,500 pints of Edglugate-Mg blood given to all classes of patients on the various hospital services.

Obviously, there are special conditions such as hyperkalemia, hemophilia, and the rare instances of Factor V deficiency in which citrated blood would be preferable. At the present time, we do not feel that Edglugate blood has any advantages over ACD for ordinary use, but we have found it satisfactory for the majority of patients.

SUMMARY

Until it becomes possible to maintain blood outside the body in a condition of normal homeostasis, there is no doubt that heparinized blood freshly drawn from the donor by meticulous technique is the most ideal blood for use in human perfusions.

In order to employ any substitute blood which has been stored even temporarily for this purpose, one must be willing to accept some changes in this blood as inevitable. In these studies we have attempted to evaluate both the advantages and disadvantages of an anticoagulant—preservative mixture designed as a substitute for fresh heparinized blood Its advantages including the possibility of having blood on hand for emergency perfusions have been outlined Its disadvantages and limitations at the end of the 5 day permissible storage period for perfusion are increased plasma potassium content and depression of antihemophilic globulin and Factor V levels In spite of these changes, we have had no recognizable difficulties in 81 perfusion cases employing Edglugate Mg blood stored up to 5 days for priming the extracorporeal apparatus We are most hopeful that continuing studies of this anticoagulant will result in further improvement of its preservation qualities for this purpose

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(For Discussion, see page 638)

AN AUTOMATICALLY CONTROLLED, INEXPENSIVE PUMP-OXYGENATOR

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SINCE the early reports of the successful development of extracorporeal circulation and open heart surgery,[8, 14] there has been widespread interest in refinement of techniques. Our group has directed its energies recently to the development of an inexpensive, self-controlled pump-oxygenator.

During the 10 years that we have been interested in experimental extracorporeal circulation, we have studied various types of pumps[10] as well as bubble oxygenators, screen- and disc-type oxygenators. At present, we prefer a rotating disc oxygenator which we have modified to suit our particular needs.

The apparatus consists of a rotating disc oxygenator originally suggested by Björk[1] and more recently, described by Kay and Cross[2, 3, 4, 11] and others,[10] combined with a roller-type pump. Venous blood is brought from the superior and inferior venae cavae to the oxygenator by gravity. Since a venous pump is not used, a significant source of trauma to the blood is eliminated. The pool of blood in the oxygenator serves as a venous reservoir so that the latter component is also eliminated. The discs are driven directly by a small fractional horse power motor at 120 revolutions per minute. Oxygenated blood leaves at the opposite end of the chamber and is carried by large-bore Tygon tubing to a roller pump. The pump then returns the blood to the arterial side through a filter. Excess blood in the opened, bypassed heart is collected by a suction tip attached to a second roller pump which delivers it to a combined defoaming chamber and bubble trap reservoir. From here, the blood is returned to the venous end of the oxygenator.

It has been shown by McCaughan and his co-workers[13] and others that most of the trauma to the blood removed from the opened heart results from excessive mixing of air with the blood in the suction pump. To minimize this effect, a control button has been placed on the suction handle which is pressed only when suction is desired. Thus the pump is turned on and off at the table, and the influx of air is minimized.

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The parts of the system which are in contact with blood consist of Tygon tubing, rubber, stainless steel, and silicone coated Pyrex glass All of the components are autoclavable, thus ensuring sterility

CONTROLS

In most centers where cardiopulmonary bypass is used clinically, the pump oxygenator has been operated by either a physician or a specially trained technician or group of technicians It is usually necessary to observe several variables continuously, and make adequate adjustments during the perfusion Among the more important factors to be observed and controlled are (1) venous pressure, (2) arterial pressure, (3) blood level in the oxygenator, (4) flow rate, (5) blood temperature, (6) replacement of blood loss, and (7) the electrocardiogram In addition, some centers routinely monitor (8) the electroencephalogram, (9) arterial and venous oxygen saturation, and (10) blood pH and pCO_2

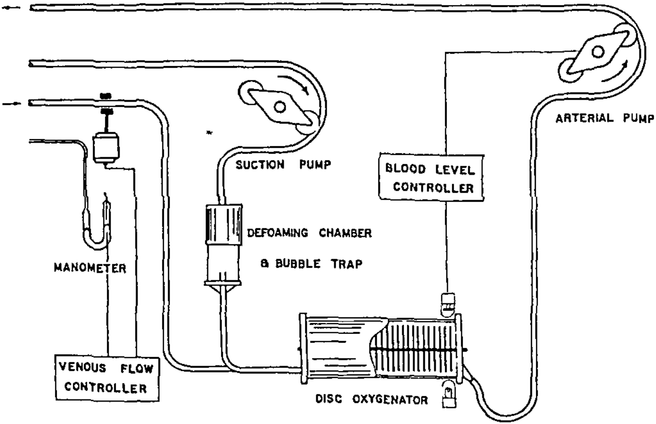

Fig 1—Schematic diagram of blood flow circuit

It is generally agreed that the continuous observation and correction of the first 7 factors are necessary for a successful perfusion By using three control systems, we are able to observe continually and maintain automatically the first 5 factors at pre set levels The technician is able, therefore, to direct his attention to the replacement of abnormal blood loss, under the direction of the anesthesiologist Gibbon[8] and Kirklin[9, 10] and their associates have described the automatic control mechanisms used in the screen oxygenator which they employ

VENOUS PRESSURE

Venous pressures are measured by passing a catheter through a superficial vein into the inferior vena cava A sealed mercury manometer is attached to the end of the catheter. Two electrodes are introduced into one limb of the mercury manometer and so placed to sense pressures of 10 cm. and 12 cm. of water. A motor-driven occluding clamp is placed on the main venous line between the heart and the input opening of the oxygenator chamber. Since the oxygenator is placed 75 cm. below the heart level, a greater negative pressure is developed at the opening of the venous line than can be used efficiently. A simple relay circuit is so arranged that if the venous pressure is below 10 cm. of water the motor is turned on to close the clamp ⅛ of a turn, thus reducing the amount of blood removed from the venae cavae. It then waits 8 seconds to see if this adjustment is sufficient to bring the venous pressure into the "normal" range. If it is not, it will make another correction and again wait 8 seconds. If the venous pressure is between 10 cm. and 12 cm. of water (our arbitrarily selected "normal" range), the motor-driven clamp remains in a fixed position. If the venous pressure is higher than 12 cm. of water, the circuit turns on the motor-driven clamp to open ⅛ of a turn, thus removing more blood from the superior and inferior venae cavae; it then waits 8 seconds and if the venous pressure has not fallen to "normal" it will then make another adjustment. This mechanism thus assures constant surveillance of the venous pressure and automatically adjusts it when indicated to ensure maintenance of normal venous pressure. Therefore, the same venous flow that would normally return to the heart is now being delivered to the pump-oxygenator.

BLOOD LEVEL CONTROL

Since reliability, autoclavability, and simplicity were the cardinal requirements in the design of the volume sensor, a means for obtaining a large output signal at useful power levels without complicated vacuum tube or transistor circuitry was sought. Methods that involve weighing the perfusion chamber, level sensors which require floats, or capacitive blood level pickup using the blood as a dielectric were rejected because of mechanical and electrical complexity.

A photoelectric blood level sensor was decided upon since it could operate outside the oxygenator chamber, eliminating cleaning and autoclaving problems. In addition, the complete generality possible with a photoelectric pickoff permits the direct application to a wide variety of oxygenator chamber designs with a minimum of modification. A light source and a light sensitive cell mounted on the outside of the oxygenator chamber are arranged so that a light beam passes through the walls of the chamber and falls upon the sensitive surface of a photocell in such a manner that changes in blood level varies the amount of the light falling on the cell. The electrical output of the cell is then used to control the speed of the arterial pump motor.

A major factor in the decision to use a photoelectric sensor was the recent advent of large area cadmium sulfide photocells of great sensitivity and capable of dissipating as much as 0.5 watt of electrical power. The output of such a cell could easily be used to control a simple power amplifier required for the 1/8 horse power variable speed pump motor.

The cadmium sulfide cell is a photoconductive cell, that is, the electrical conductivity of the cell varies with the amount of light falling on it. As a circuit element, it behaves like a variable resistor. The type 6957 used in this system is a hermetically sealed unit in which the resistance varies from many millions of ohms when dark to a few hundred ohms when illuminated. The purpose of the photoelectric flow controller is to maintain a fixed volume of blood in the oxygenator throughout the procedure. This state of equilibrium is achieved by automatically adjusting the speed of the arterial pump which withdraws blood from the oxygenator. The pumping rate varies in response to signals from the sensor, the output of which is a function of the blood volume in the oxygenator. An increase in volume of blood in the oxygenator results in an increased withdrawal pumping rate, and a decrease in volume reduces the pumping rate. The photocell is thus able to "watch" the blood level changes in the oxygenator precisely. In the 17-inch disc oxygenator, an increment of 50 c.c. of blood is detectable by the photocell The electrical system is damped and is extremely stable. The photocell tends to select the correct pump speed continuously and maintain this speed at all times. The arterial pump output is determined by the venous return to the oxygenator The venous return, as has been described earlier, is selected automatically to maintain venous pressures at normal levels. The blood level, then, in the pump-oxygenator is effectively locked and thus (barring abnormal blood loss from the entire system) ensures against undesirable shifts in the patient's blood volume[6, 7, 15] and automatically maintains blood pressures within normal ranges. Normal arterial

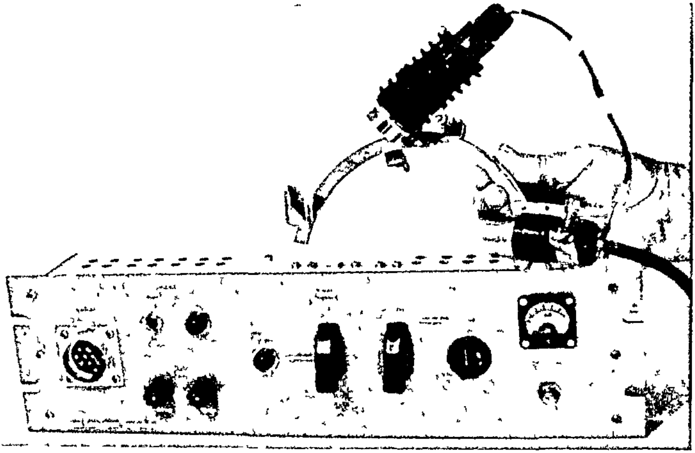

Fig 2—Special clamp with photoelectric cell and light source, and electronic control unit

pressures assure flow rates which are consistently above 100 c.c. per kilo per minute. Thus, this one sensing device and control mechanism automatically maintains the blood in the machine at pre-set volumes, the flow rates above 100 c.c. per kilo per minute, and the arterial pressures within the normal range.

Falling arterial pressures indicate abnormal blood loss from the entire system. Blood replaced into the oxygenator will then be delivered immediately to the patient, and arterial pressure will return to the normal range. Provision is made for quickly switching the control to manual operation in case of failure, by disconnecting the cell and substituting a variable resistor. The only components in the controller having finite life are two thyratrons and the excitor lamp. The thyratrons used have sufficient capacity so that if one fails, the system will continue in operation. The possibility of both thyratrons failing simultaneously is remote. Failure of the excitor lamp will cause the pump to run at full speed. In this event, the control is switched to manual operation for the remainder of the perfusion. Two excitor lamps could be built into the lamp housing for additional safety. This controller should have excellent reliability and should not be subject to sudden failure since it is simple in design and contains components that inherently have long life.

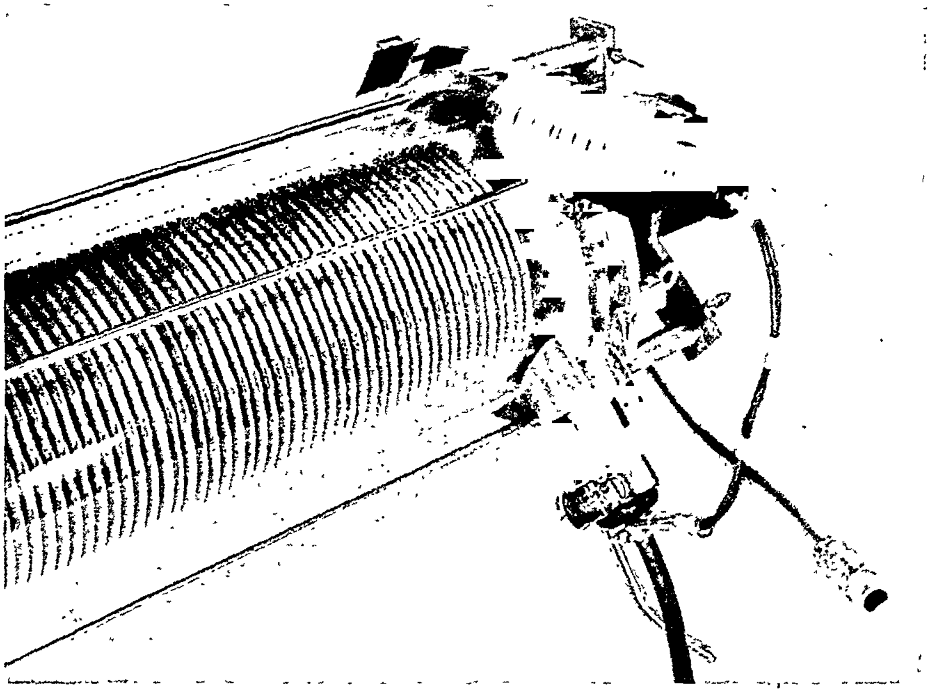

Fig. 3.—Special clamp with photoelectric cell and light source mounted on oxygenator.

BLOOD TEMPERATURE CONTROL

It has been shown by De Wall[5] and others that it is desirable to maintain the blood in the extracorporeal circuit close to normal body temperatures. First, rapid changes in blood temperature tend to promote hemolysis of blood, and second, oxygen is more soluble in blood at lower temperatures than at higher body temperatures. Therefore, it is possible that a saturated solution of oxygen in cooler blood in the oxygenator may come out of solution in the form of small bubbles when the blood is returned to the patient and becomes warmed. A thermistor probe is placed in a thin-walled pocket in the oxygenator chamber below the blood level. The temperature of the blood is then sensed by the thermistor and controlled by a commercially available temperature switch which turns a heater coil on and off. We have set the controller to 38° C. and are able to maintain the blood temperature within 0.5° C. The controller itself can detect changes of 1/10 of a degree centrigrade.

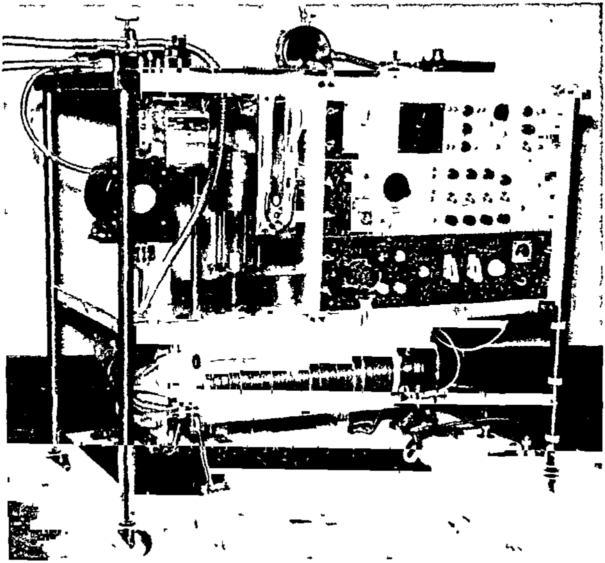

Fig 4 —Completely assembled automatically controlled pump-oxygenator

TECHNIQUE OF PERFUSION

The pump oxygenator is primed with 2,500 c c of blood This amount is sufficient to fill the oxygenator, the combined filter and bubble trap, the defoaming chamber, and all of the lines. Blood is circulated for a few minutes in order to be certain that all air bubbles have been removed. The arterial pump motor is turned off by a switch The arterial and venous lines are then clamped and appropriate connections are made to the patient To start the perfusion, the clamps are removed from the venous and arterial lines and the arterial pump motor switch is turned on. From that point on, the pump-oxygenator regulates itself. When the tourniquets around the superior and inferior venae cavae are tightened to initiate total bypass, the increased venous return to the pump-oxygenator is automatically compensated for and all of this blood immediately returned to the patient after oxygenation. To discontinue the perfusion, one needs only to clamp the venous line. Venous return to the pump-oxygenator is then discontinued and the arterial pump will come to a stop as soon as the blood level in the oxygenator reaches its priming position.

DISCUSSION

It seems axiomatic that if a mechanism can be made to perform a given function more reliably than a human being that it should be used. A practical consideration that often enters in such a decision is the cost of such an apparatus. All of the electronic controls in our pump-oxygenator can be purchased for under $1,000.* The technician who stands by during the bypass has to be available in case of mechanical or electrical failure, in which case the pump-oxygenator can be run by manual controls. Otherwise, after the initial filling of the oxygenator with priming blood, he can devote his entire attention to replacement of unusual blood loss under the direction of the anesthesiologist.

Adjustments during the perfusion are automatically sensed and made by the machine during critical periods of change. When the perfusion is first begun, there is a tendency for the pump to overtransfuse the patient. When the venae cavae are occluded, an increased amount of blood is usually returned to the pump-oxygenator. Conversely, when the tourniquets are released, large amounts of blood can suddenly be lost from the machine. If there is unusual blood loss from the patient during the bypass, there is a tendency for blood to be lost from the pump-oxygenator. If vasopressor drugs are given, blood has a tendency to rise in the oxygenator. We feel that these abnormal shifts in blood volume are deleterious to the patient on bypass and are avoided when the blood volume in the machine is maintained at a constant level. Decreased blood level in the oxygenator decreases the efficiency of the oxygenating surface and, if the level drops low enough, may lead to air embolism. If the blood in the oxygenator rises too high, it may wet the shaft, leading to turbulence and foaming, or leak out of the shaft bearing. The apparatus that we have designed eliminates the possibility of the occurrence of these untoward manifestations.

SUMMARY

1. An improved, automatically controlled, rotating disc pump-oxygenator is described.

2. Venous pressures are continuously monitored and automatically controlled during bypass by the use of a motor-driven clamp on the venous line.

3. Blood levels, arterial pressures, and blood flows are automatically sensed and controlled with one device which is rugged, reliable, and inexpensive.

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*Available from the Teca Corporation, 80 Main Street, White Plains, N. Y.

4. Blood temperatures in the oxygenator are also controlled automatically.

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(For Discussion, see page 638)

AN EXTERNALLY VALVED HYDRAULIC CARDIAC SUBSTITUTE

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INTRODUCTION

In applying the techniques of extracorporeal circulation, cardiac pumps pose less of a problem in perfusions than do the oxygenator systems. Using the Sigmamotor pump, which is perhaps the most traumatic of all the commonly used machines, Lillihei and DeWall[1] express satisfaction with the amount of hemolysis produced during an average perfusion. And yet, as time goes on, and surgical bypass time increases, as more complex intracardiac defects are dealt with surgically, and as we approach the new era of medical bypass to support the failing heart, better pumps will be needed.

Four basic requirements must be met in the design of the ideal pump.[2]

1. The pump ventricle and inflow and outflow tracts should be uniform, with relatively large internal diameters.
2. All tubing surfaces in contact with blood should be mirror smooth, plastic in nature, free of turbulence, without internal valving, and be easily cleaned.
3. A variable flow from 0 to 5,000 c.c. per minute must be available which can be varied as to stroke volume and pulse rate. It should be possible to vary this flow either manually or by servomechanisms tied to either the oxygenation system or the patient's electrocardiograph.
4. Constant information should be available as to the pump volume flow and the patient's arterial and venous pressure. To ensure an accurate pump output, there should be minimal pump load sensitivity as smaller cannulas are selected and/or as peripheral resistance rises.

For practical purposes there are three types of pumps currently employed.

1. *Dale-Schuster*[3-6]—in which a ventricle is externally compressed, but not to total occlusion, and unidirectional flow is obtained by internal valving either with butterfly or ball valves, or by external valving with some form of pressure bar or point which is occlusive.

2. *Sigmamotor*[7]—in which travelling compression waves are set up in a ventricle by unidirectional rollers which are almost or completely occlusive.

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3. *De Bakey*[8]—in which travelling compression waves are produced in a ventricle by unidirectional rollers which are almost or completely occlusive.

If at some point in any of these systems there does not exist complete occlusion, the pumps become load sensitive to some degree and lose their ability to pump a constant volume of blood under all conditions of resistance. There are many perfusionists who feels strongly that it is not necessary to make their pumps occlusive. Rather than depend on a knowledge of accurate flow, they monitor systemic arterial pressure. It appears, however, that the only simple way that a pump can be constructed to be nonload sensitive is for it to be occlusive. On the other hand, as the occlusive area wiped or compressed per unit flow rate increases, so will hemolysis increase.

We have studied anew the problems relating to development of a more ideal pump and wish to present one solution to the problems just outlined. Our pump acts on an externally compressed nonocclusive ventricle of uniform Tygon tubing. The external valves act on the same piece of Tygon which is functioning as the ventricle. The tubing from the pump inlet to the outlet is uniform in diameter and without joints.

Our initial model was designed to evaluate the feasibility of some of the mechanisms proposed for a clinical pump and to provide a unit for performing hemolysis tests under varying conditions.

DESCRIPTION OF THE PUMP*

Pumping action is achieved by hydraulically squeezing a Tygon ventricle located between two mechanically actuated guillotine-type valves (Fig. 1). The valves and pumping action are synchronized so that the outlet valve opens as the Tygon is squeezed and the inlet valve opens as the Tygon returns to its normal shape. Thus, for one half cycle the pump is delivering fluid and for the other half cycle the ventricle is filling.

The hydraulic pressure, compressing the ventricle, is applied as follows: The Tygon ventricle is surrounded by a fluid-filled, annular chamber that uses a slightly larger diameter Tygon tube as its inner wall. The outside diameter of the ventricle and the inside diameter of the hydraulic chamber are essentially the same. Fluid is delivered to and taken from the annular chamber by the mechanical actuation of a rubber diaphragm located on an auxiliary chamber which is hydraulically connected to the annular chamber. The two chambers form a closed, sealed hydraulic unit with no possibility of leakage into the blood containing ventricle. A positive hydraulic action in the annular chamber is assured that is directly proportional to the mechanical action on the diaphragm of the auxiliary chamber. The mechanism is arranged so that at no time does the Tygon ventricle become occlusive.

Valving action is achieved by occlusively squeezing the ventricle tubing with transverse rods, ¼ inch in diameter, externally located 1 inch from the ends of the annular chamber. The valves are actuated through lever arms connected to cams located on the main-drive shaft. The eccentric, which operates the diaphragm actuating mechanism, is also on the main-drive shaft, thus ensuring positive synchronization between the valves and pumping action.

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*Manufactured by The United Precisioneers Inc., Calabasas, Calif.; distributed by The Mark Co., Randolph, Mass.

The pump is driven by a model M143 Zero-Max variable speed drive and motor. A belt with a three-to-one pulley reduction is used, giving available pulse rates of zero to 130 pulses per minute. The Zero-Max speed control is used to vary the pulse rate. A mercury switch, to eliminate sparking, is used for the main power switch. Separate control knobs adjust the pulse rate and the stroke volume independently of one another. The flow rate can be varied from zero to full flow by changing the pulse rate and/or by changing the stroke volume while the pump is stopped or in operation.

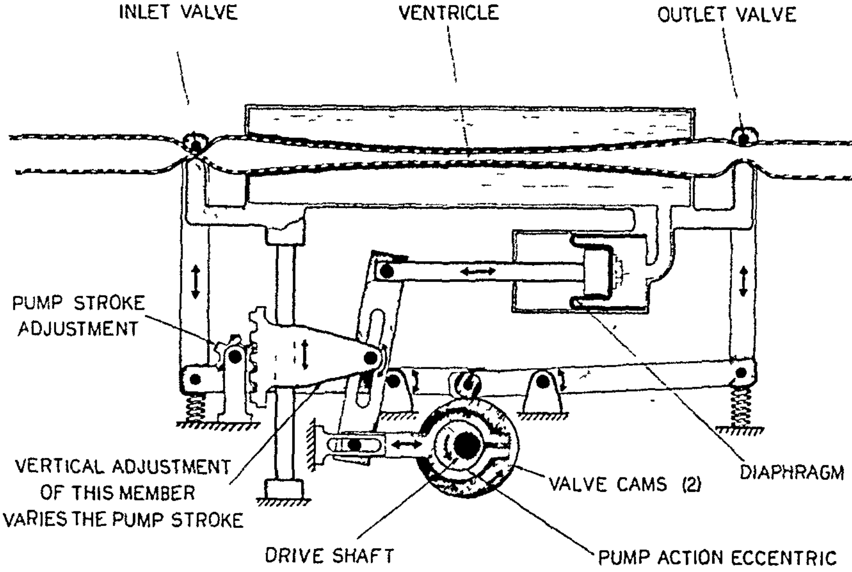

Fig. 1.—Diagrammatic sketch of the hydraulic pump principle. Note that the drive shafts actuating the hydraulic cylinder and the arms to the guillotine valves are synchronous and mechanically linked.

Using a 12-inch ventricle length with a ⅛ inch wall and an internal diameter of ¾ inch, a maximum flow of 5,800 c.c. per minute at a pulse rate of 114 was obtained. This flow can be easily increased by using a larger ventricle. The pump is self priming and is essentially not load sensitive. It has been run continuously in one test for over 50 hours at 100 pulses per minute using the same ventricle, without producing noticeable damage to the Tygon tubing and without altering the pumping characteristics.

A second pump has been designed and tested using a mechanical pressure bar instead of hydraulic fluid to compress the ventricle. Since the ventricle is not occluded by the pressure bar and all other aspects of the pump were kept constant, we could find no essential difference in the performance between the hydraulic and mechanical ventricles.

A third pump, which is the clinical unit, was prepared utilizing identical but refined principles outlined in this paper but with a mechanical compression bar acting on the ventricle.

TEST METHOD

In order to evaluate the described pump, comparative hemolysis tests were concurrently performed with De Bakey,* Sigmamotor, and the UPI pumps. Freshly drawn, heparinized dogs' blood from several animals was premixed in a plastic container from which equal volumes were taken for each of the test pumping circuits. The blood was placed in identical plastic test chambers and circulated through identical circuits until each pumping circuit was free of air. Control bloods were taken after the circuits were filled and free of air; thereafter the pumps were operated for varying test periods as required. For each study, the test chambers were kept of uniform size, shape, and position and all adapters and orifices were of uniform size so that all tests and pumps can be directly compared.

Plasma hemoglobin, proteins, fibrinogen, and platelets were monitored during the tests. The results obtained from electrophoretic protein determinations were so equivocal as to exclude them from presentation. Likewise, the heparin effect rendered platelet and fibrinogen determinations so inaccurate that they had no comparative validity in our study.

We relied, therefore, on plasma hemoglobin determinations as our most accurate criterion of blood damage. The determinations of plasma hemoglobin were done spectrophotometrically using the Beckman DU spectrophotometer with readings at 540 and 570 $m\mu$, the results being averaged.

The following studies were accomplished: (a) pulse wave and pressure recordings were taken proximal and distal to each ventricle and also within the UPI pump ventricle, (b) load sensitivity determinations, and (c) hemolysis with both open lines and with constriction. Our basic pump principles were then reevaluated and a clinical pump designed and fabricated.

RESULTS

Pressure Characteristics.—Many combinations of flow rate and cannula size were tested; however, data are presented herein only for combinations that are representative of most common conditions under which pumps would be operating.[10]

A comparison of pressure wave forms of all three pumps at a flow rate of 3,000 c.c. per minute, pumping through a 0.25 inch constriction, is presented in Fig. 2. Pressures were obtained from each pump distal and proximal to the ventricles; in addition, it was possible to obtain ventricle pressures in the UPI pump.

De Bakey: The peak pressure range was +50 mm. Hg to –75 mm. Hg at 48 pulse rate. The inlet line wave form was sinusoidal and damped over the duration of the cycle with a negative mean pressure. The outlet line wave form was a very shallow sine wave superimposed on the mean positive pressure. During only a small part of the cycle is the outflow pressure less than zero which indicates that this pump is, in a sense, the least pulsatile of the three studied.

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*Designed and kindly furnished for tests by Peter F. Salisbury, M.D.

Sigmamotor: The pressure range was +170 mm. Hg to −160 mm. Hg at 125 pulse rate. The inlet wave form was a single sine wave with the positive pressure shape distorted due to the action of the finger cams. The outlet wave form was a single sine wave with the entire wave distorted by a higher frequency smaller amplitude wave also produced by the action of the finger cams.

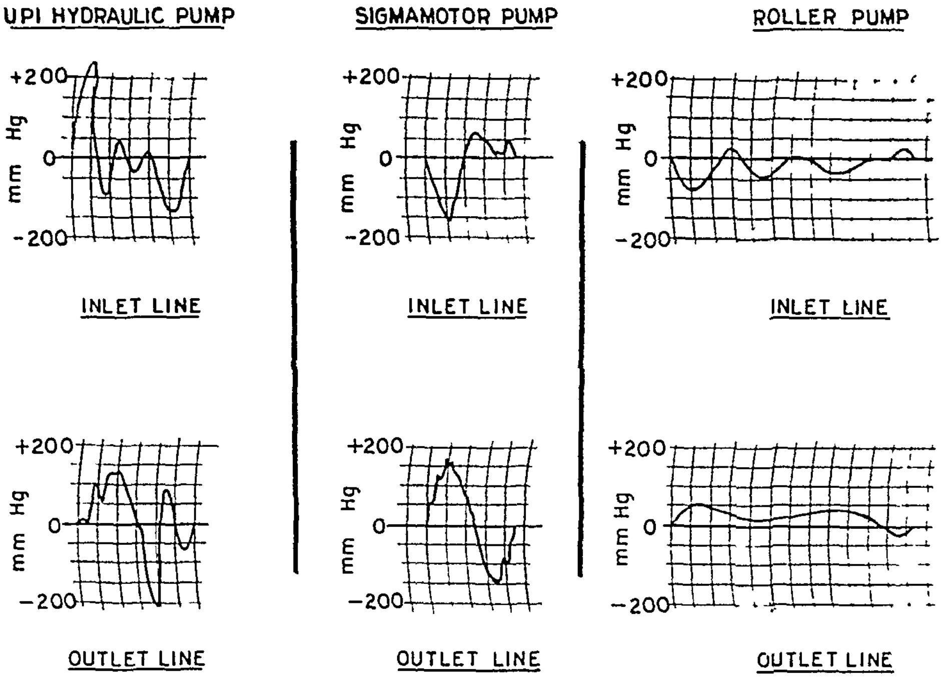
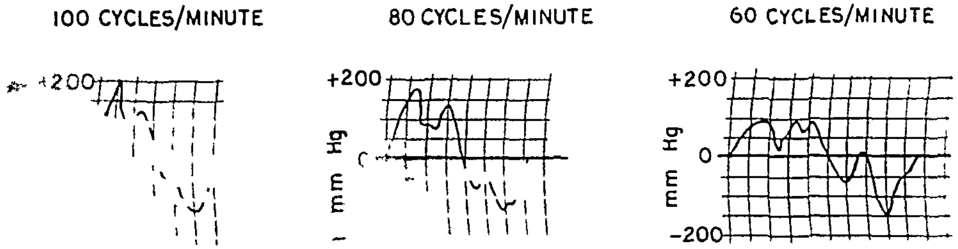


Fig. 2.—Comparative ventricle pressure wave forms for single cycles at 3,000 c.c./min. flow with outlet line constricted to 0.250 inches in diameter.



Fi 've wave UPI pump for single cycles at 3,000 c.c./min.
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the physiologic range.

The UPI pump ventricle pressures at 3,000 c.c. per minute, pumping against a 0.25 inch restriction at pulse rates of 60, 80, and 100 per minute are given in Fig. 3. It was found that as the pulse rate increased there was a parallel increase in intraventricular pressure. In considering two identical total volume flows per unit time, each with a different pulse rate, the higher pulse case requires higher fluid accelerations and, therefore, results in higher peak pressures. This effect is clearly shown in Fig. 3.

Load Sensitivity and Pressure Response to Load.—When all three pumps were set just occlusive, there was little difference in drop of minute volume output under constriction. The UPI pump showed the greatest load sensitivity of the three pumps tested but the maximum drop in flow for a 3/16 inch cannula at 3,000 c.c. per minute was less than 3 per cent (Table I).

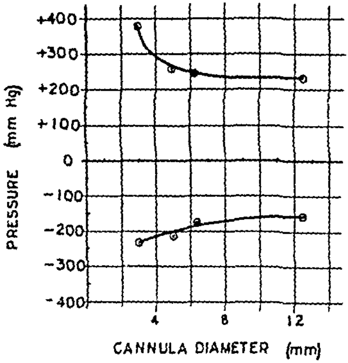

Fig. 4.—UPI pump ventricle pressure vs. cannula size at 3,000 c.c./min. flow rate and 100 cycles per minute pulse rate.

TABLE I. LOAD SENSITIVITY COMPARISON FOR VARIOUS TYPE PUMPS*
(PER CENT DROP IN FLOW AT 3,000 C.C./MIN.)

RESTRICTION (CANNULA I.D.)	UPI PUMP (HYDRAULIC) (% DROP IN FLOW)	SIGMAMOTOR PUMP (% DROP IN FLOW)	ROLLER PUMP (% DROP IN FLOW)
None	0.00	0.00	0.00
¼ inch	1.50	1.00	0.50
3/16 inch	2.90	1.60	0.75
⅛ inch*	6.60	2.45	2.00
Pulse rate	100	126	48

Load Sensitivity: At flow rates of 1,000 c.c./min. with a ⅛ inch cannula and at flow rates of 3,000 c.c./min. with a ¼ inch cannula, all pumps being occlusive, there was no appreciable drop in the flow rates from pre-set levels.

**NOTE:* The work of Reference 2 indicates that for flows of 3,000 c.c. per minute cannulas should be no less than ¼ inch internal diameter.

Since the UPI pump ejects fluid during only one half of each pumping cycle, its pumping characteristics are more sharply pulsatile than either the De Bakey or the Sigmamotor pumps. A family of curves were studied (Fig. 4 being representative) of intraventricular pressures produced while pumping through cannulas of gradually decreasing inside diameter at constant minute

Sigmamotor: The pressure range was +170 mm. Hg to −160 mm. Hg at 125 pulse rate. The inlet wave form was a single sine wave with the positive pressure shape distorted due to the action of the finger cams. The outlet wave form was a single sine wave with the entire wave distorted by a higher frequency smaller amplitude wave also produced by the action of the finger cams.

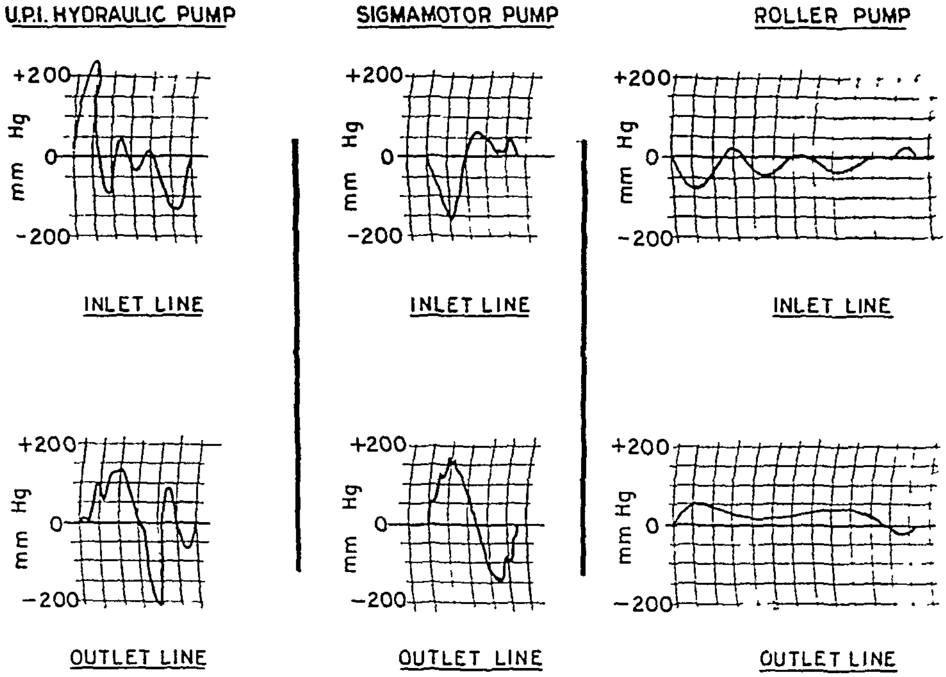

Fig. 2.—Comparative ventricle pressure wave forms for single cycles at 3,000 c.c./min. flow with outlet line constricted to 0.250 inches in diameter.

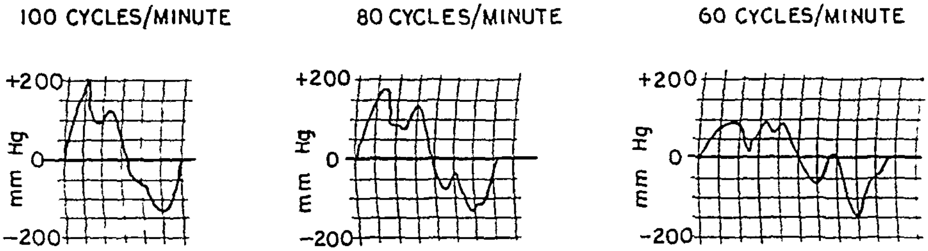

Fig. 3.—Comparative wave forms of the UPI pump for single cycles at 3,000 c.c./min. at pulse rates of 60, 80, and 100 cycles per minute. Note that the slower the pulse rate the lower is the intraventricular pressure.

UPI: There was a pressure range of +250 mm. Hg to −210 mm. Hg at 100 pulse rate. The inlet and outlet line wave forms were essentially similar. The pressure wave distortion could have been due to the elastic characteristics of the Tygon tubing which was free to absorb and release energy in the ventricle. Under the test conditions this pump developed the highest measured pressures. Since the ventricle fills during one half the cycle and pumps during the other half, a higher pressure is required than in either of the other two pumps at near the maximum pulse rate. However, the most adverse pump system pressures encountered were within the upper limits of the physiologic range.

The UPI pump ventricle pressures at 3,000 c.c. per minute, pumping against a 0.25 inch restriction at pulse rates of 60, 80, and 100 per minute are given in Fig. 3. It was found that as the pulse rate increased there was a parallel increase in intraventricular pressure. In considering two identical total volume flows per unit time, each with a different pulse rate, the higher pulse case requires higher fluid accelerations and, therefore, results in higher peak pressures. This effect is clearly shown in Fig. 3.

Load Sensitivity and Pressure Response to Load.—When all three pumps were set just occlusive, there was little difference in drop of minute volume output under constriction. The UPI pump showed the greatest load sensitivity of the three pumps tested but the maximum drop in flow for a ³⁄₁₆ inch cannula at 3,000 c.c. per minute was less than 3 per cent (Table I).

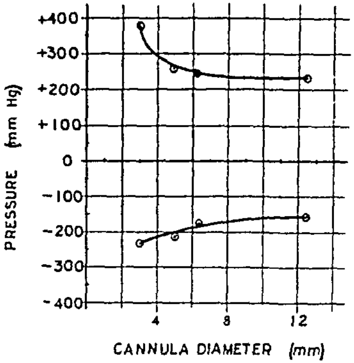

Fig. 4.—UPI pump ventricle pressure vs. cannula size at 3,000 c.c./min. flow rate and 100 cycles per minute pulse rate.

TABLE I. LOAD SENSITIVITY COMPARISON FOR VARIOUS TYPE PUMPS*
(PER CENT DROP IN FLOW AT 3,000 C.C./MIN.)

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None	0.00	0.00	0.00
⅛ inch	1.50	1.00	0.50
³⁄₁₆ inch	2.90	1.60	0.75
¼ inch*	6.60	2.45	2.00
Pulse rate	100	126	48

Load Sensitivity. At flow rates of 1,000 c.c./min. with a ⅛ inch cannula and at flow rates of 3,000 c.c./min. with a ¼ inch cannula, all pumps being occlusive there was no appreciable drop in the flow rates from pre-set levels.

**NOTE.* The work of Reference 2 indicates that for flows of 3,000 c.c. per minute cannulas should be no less than ¼ inch internal diameter.

Since the UPI pump ejects fluid during only one half of each pumping cycle, its pumping characteristics are more sharply pulsatile than either the De Bakey or the Sigmamotor pumps. A family of curves were studied (Fig. 4 being representative) of intraventricular pressures produced while pumping through cannulas of gradually decreasing inside diameter at constant minute volume. This characteristic might suggest the use of a simple pressure surge chamber to reduce peak pressures for extra high flow rates and small diameter cannulas.

The safe lower limits of cannula size were taken from the work of Clowes and his associates[11] in which it was shown that the upper limits of safe flow were: 3 mm. cannula, 650 c.c. per minute; 5 mm. cannula, 1,800 c.c. per minute; and 8 mm. cannula, 3,400 c.c. per minute. It was found that the intraventricular pressures of the UPI pump did not exceed physiologic limits when examined under these conditions.

The flow rates in the De Bakey and Sigmamotor pump are primarily dependent on pulse rate. In the case of the De Bakey pump, pulse rates approach a normal value for high flow rates and are quite low for smaller minute volumes.

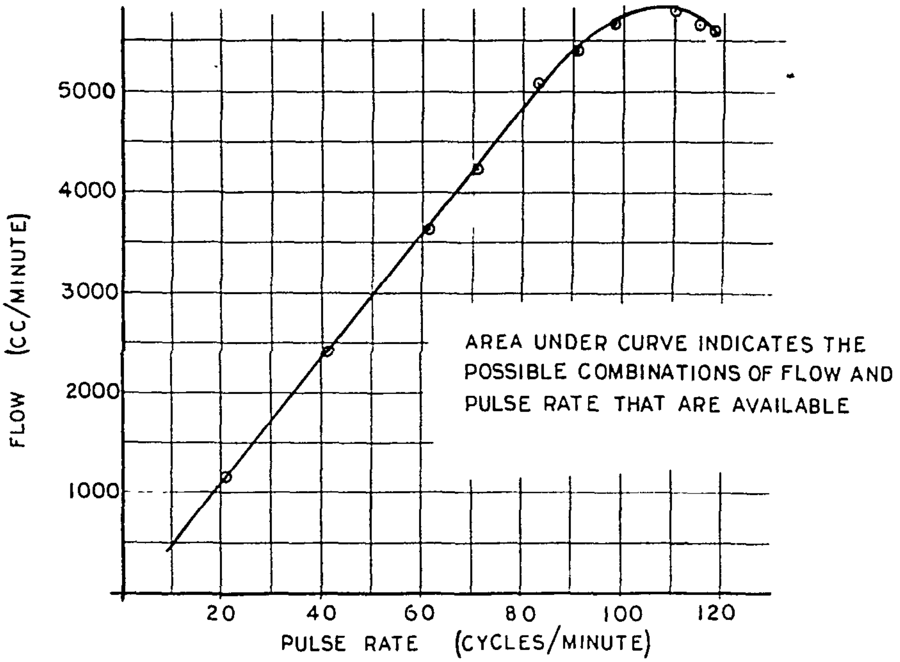

Fig. 5.—Illustrates the combinations of flow rates and stroke adjustment that are available with the UPI pump.

On the other hand, the Sigmamotor pump develops a pulse that is very rapid at high flow rates. Between 0 and 3,000 c.c. per minute, the UPI pump is capable of functioning at any selected pulse rate between 50 to 120 cycles per minute (Fig. 5). The pulse ranges as a function of volume flow rate for all three pumps can be seen in Table II which clearly indicates the versatility of pulse rate for the UPI pump.

TABLE II. PULSE-FLOW CHARACTERISTICS FOR VARIOUS TYPE PUMPS

TYPE OF PUMP	PULSE RANGE AT FLOW RATE OF		
	1,000 C.C./MIN.	3,000 C.C./MIN.	4,500 C.C./MIN.
De Bakey	20	48	74
Sigmamotor	45	125	180
UPI (hydraulic)	19 to 120	50 to 120	75 to 120

Hemolysis.—All three pumps were tested under two conditions: (a) at flow rates of 3,000 c.c. per minute with no line constriction and with a simple plastic reservoir in the circuit (the total system volume circulated was 800 c.c.), (b) at flow rates of 2,400 c.c. per minute with a 0.25 inch I.D. cannula restriction in the line (the circuit included a debubbling chamber of stainless steel sponge and contained a total system volume of 1,000 c.c.).

Although a flow rate of 3,000 c.c. per minute could be achieved by the UPI pump in a variety of ways, that is, with a single or double ventricle and at any pulse from 50 to 120 cycles per minute, we chose conditions which would seem to be as unfavorable as possible. Therefore, the UPI pump was tested with a single ventricle and at the higher pulse rates.

The UPI hydraulic pump was considerably less traumatic to blood than the other two pumps tested. Under conditions of no line constriction, the UPI pump was twofold less traumatic to blood than the De Bakey and four and a half times less traumatic to blood than the Sigmamotor pump. When a line constriction was placed in the circuit, the difference was even more marked. The UPI pump was fourfold less traumatic than the De Bakey and twenty-seven times less traumatic than the Sigmamotor pump (Table III).

TABLE III. CIRCULATING TIME 2 HOURS*

TYPE OF PUMP	PUMPS DELIVERING 3,000 C.C./MIN. INTO SIMPLE RESERVOIR (TOTAL SYSTEM VOLUME 800 C.C.)			PUMPS DELIVERING 2,400 C.C./MIN. THROUGH A ¼ IN. CONSTRICTION INTO DEBUBBLING CHAMBER (TOTAL SYSTEM VOLUME 1,000 C.C.)		
	MG. % FREE HBG	TOTAL GM. FREE HBG	INDEX OF HEMOLYSIS	MG. % FREE HBG	TOTAL GM. FREE HBG	INDEX OF HEMOLYSIS
UPI	31	0.248	0.069	14	0.140	0.043
De Bakey	62	0.496	0.138	60	0.600	0.173
Sigmamotor	144	1.152	0.320	384	3.840	1.331

*Index of comparative hemolysis between the UPI, De Bakey, and Sigmamotor pumps operating under identical conditions. Note that the UPI pump causes from 2 to 27 times less hemolysis than the other two pumps studied. Index of Hemolysis = mg. free Hbg produced per 100 c.c. of flow.

To determine the effect of varying the pulse and flow rates of the UPI pump, 800 c.c. of freshly drawn dog blood was circulated through a simple reservoir for a period of 1 hour. Studies were made at pulse rates of 60, 80, and 100 cycles per minute and at volume flows of 1,500, 3,000, and 4,500 c.c. per minute. Inspection of Table IV shows that there was little change in the

TABLE IV. ONE HOUR CIRCULATING TIME—800 C.C. CIRCULATING VOLUME*

TYPE OF PUMP	FLOW RATE (C.C./MIN.)	TOTAL FLOW (C.C.)	PULSE RATE (CYCLES/MIN.)	HBG CONCENTRATION AFTER 1 HOUR (MG./100 C.C.)	TOTAL FREE HBG (MG.)	INDEX OF HEMOLYSIS (MG./100 C.C. OF FLOW)
UPI	1,500	900×10^2	80	13	104	0.116
UPI	3,000	$1,800 \times 10^2$	60	13	104	0.058
UPI	3,000	$1,800 \times 10^2$	80	13	104	0.058
UPI	3,000	$1,800 \times 10^2$	100	12	96	0.053
UPI	4,500	$2,700 \times 10^2$	80	18	144	0.053
		$1,800 \times 10^2$	48	25	200	0.111
		$1,800 \times 10^2$	125	102	816	0.453

*[illegible] hemolysis of the UPI pump at a sampling of different pulse and flow rates with no line constriction. Hemolysis is almost negligible.

Index of Hemolysis under different conditions and, under all conditions tested, the UPI pump was less traumatic to the circulating blood than the other two pumps under similar conditions.

Clinical Pump.—On the basis of these laboratory studies a clinical pump was designed and fabricated (Fig. 6).

This model consists of three parallel ventricles with pumping strokes 120 degrees out of phase with each other. Three Tygon tubes are held in place by an easily removable cover. The pumping and valving action is achieved by members acting against the Tygon tubing from the under side, compressing it against the cover.

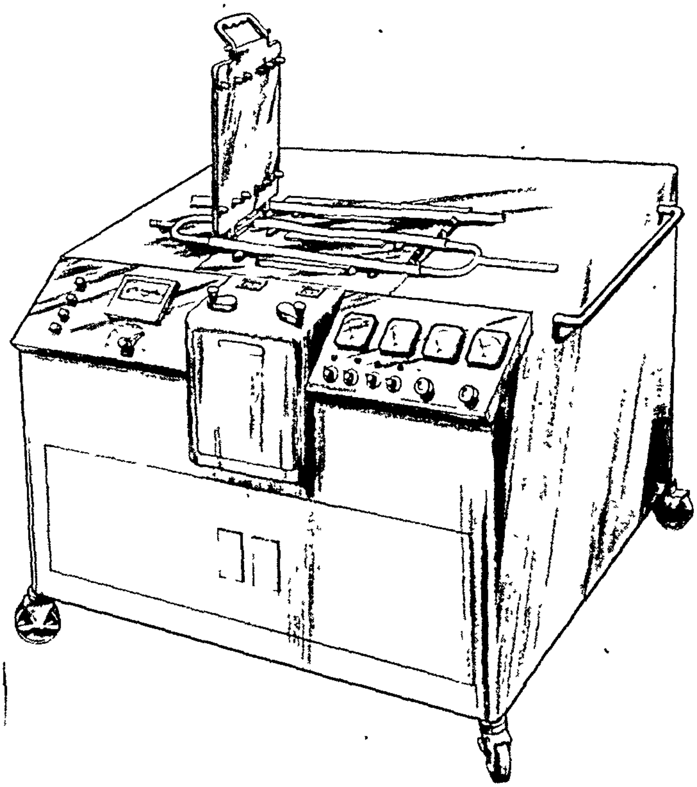

Fig. 6.—Clinical version of UPI pump with mechanical linkage, nonocclusive pressure plates, and occlusive guillotine pressure-valve bars mounted in a console with related ancillary equipment.

The ventricles are compressed by mechanical pressure bars and as was pointed out earlier, there was no difference noted in performance between nonocclusive mechanical and hydraulic compression. The valving action is the same as described in the experimental model.

A single direction clutch has been added to permit emergency hand cranking in the event of power failure. Small hand wheels control the length of the pressure plate travel against the ventricle; turning the wheel varies the flow per ventricle from zero to 4,000 c.c. per minute. The two main ventricles are controlled by a single wheel so that they may be connected in parallel for high flow rates up to 8,000 c.c. per minute. The other ventricle is controlled by the second hand wheel and may be used independently for either suction or coronary perfusion. Other basic controls consist of the usual electrical circuits and a pulse control adjustment for the variable speed drive.

This design has, as an integral part of its construction, provision to tie servomechanisms into the various components which can make the pumping action automatic within the system or synchronous with the patient's own cardiac output. This ancillary equipment, monitoring devices, and servomechanisms will be the subject of another communication.

CONCLUSIONS

We found that external compression without occlusion on a ventricle would appear to be the least traumatic method of pumping blood that we studied. Such a system requires valving at each end of the ventricle and the simplest arrangement with the least occluding surface is the pressure bar, guillotine valve. We have utilized mechanical linkages and control methods which makes the entire pump more reliable than either hydraulic or electronic linkages and/or controls.

This pumping mechanism is virtually fail-safe, trouble free, and is at least two to four times less traumatic to blood than other pumps studied. Pulse rate and stroke volume are individually variable. The pump is so designed that it may be incorporated in combination with servomechanisms.

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(For Discussion, see page 638.)

PHYSIOLOGIC P-WAVE CARDIAC STIMULATOR

Sam E. Stephenson, Jr., M.D. (by invitation), W. H. Edwards, M.D. (by invitation), P. C. Jolly, M.D. (by invitation), and H. W. Scott, Jr., M.D., Nashville, Tenn.

In 1862, Walshe[1] suggested the possibility of external control of the cardiac rate. This suggestion lay practically dormant until Zoll and co-workers,[2] in 1953, described the use of an artificial external cardiac pacemaker for treatment of the Stokes-Adams syndrome.

Analysis of the fatalities following intracardiac surgery, especially the repair of interventricular septal defects, utilizing extracorporeal circulation revealed that atrioventricular dissociation was one of the major problems leading to death in the postoperative period. Detailed studies on the relation of the bundle of His to the septal defect yielded some helpful suggestions as to the placement of sutures to avoid the conduction system but did not negate the problem.

Weirich,[3] working at the University of Minnesota, reported in 1957 the use of a timed external pacemaker functioning through a ventricular electrode to stimulate the heart through the critical postoperative period. Many others have utilized this method to treat postsurgical heart block.

We have been interested in the same problems but have felt that a more physiologic control of ventricular rate would be desirable and thus cardiac output would adjust automatically to such variations as temperature elevation, ambulation, and exercise in the postoperative period.

Feeling that the inherent mechanism to control cardiac rate in the intact individual would be difficult to improve on, we have constructed an instrument which utilizes the auricular p wave to trigger a ventricular stimulator and thus produce a sinus rhythm through an extracorporeal system substituting for the A-V node and bundle of His.

DESCRIPTION OF THE APPARATUS

The basic component of the artificial system is a modification of a muscle potential amplifier originally developed by Montgomery at this institution and designed to control an artificial ventilatory device.[4, 5, 6] This control unit is

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sensitive to impulses as low as 0.5 microvolt and contains satisfactory electronic filters to block extraneous impulses arising from external magnetic fields and artifacts. The control unit amplifies the electrical potential of auricular contraction picked up by an insulated wire lead sutured to the auricular myocardium. The amplifier processes these potentials to produce a control voltage corresponding in time with the p wave.

In operation this control voltage is modified to trigger a monostable multivibrator. The first stage vibrator acts as a variable delay unit with an adjustment from 0 to 1 second. This variable allows adjustment of the delay to correspond to the normal conduction time of the bundle of His (0.18 second). The amplified p wave is also used to trigger the sweep of a monitor oscilloscope for either the action of the amplifier or the stimulator output. The output of the delay circuit is fed into another monostable multivibrator which is capable of producing a square wave output of variable duration with a range of 0 to 1 second. This duration adjustment is usually maintained at a little less than 0.1 second which is the time normally required for stimulation of the ventricle.

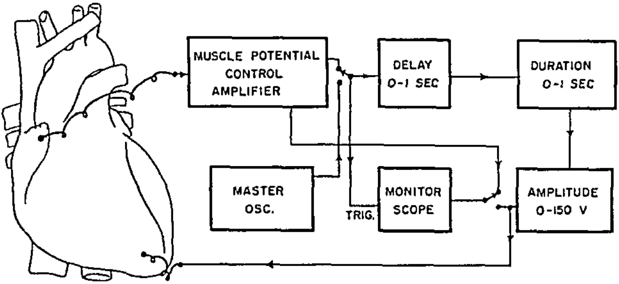

Fig. 1.—Block diagram of the p-wave cardiac stimulator showing areas of electrode insertion.

A variable output of from 0 to 150 volts is available on the unit and this can be controlled by selecting the minimal stimulus to which the ventricle will respond. (The standard Grass model S4E laboratory stimulator fills all the requirements set forth and functions smoothly as the stimulator component of the circuit.) A master oscillator is included as an emergency trigger source in case of difficulty arising with the auricular pickup or in case of complete asystole (Fig. 1).

METHODS

Unselected mongrel dogs of 6 to 16 Kg. in weight were prepared under aseptic conditions. A right thoracotomy was performed and the bundle of His was identified by passing an insulated needle through the right auricular wall into the septum. The conduction system was destroyed by an electrocoagulation technique (to be published). After satisfactory idioventricular rhythm was established, braided wire electrodes were attached by means of mattress sutures

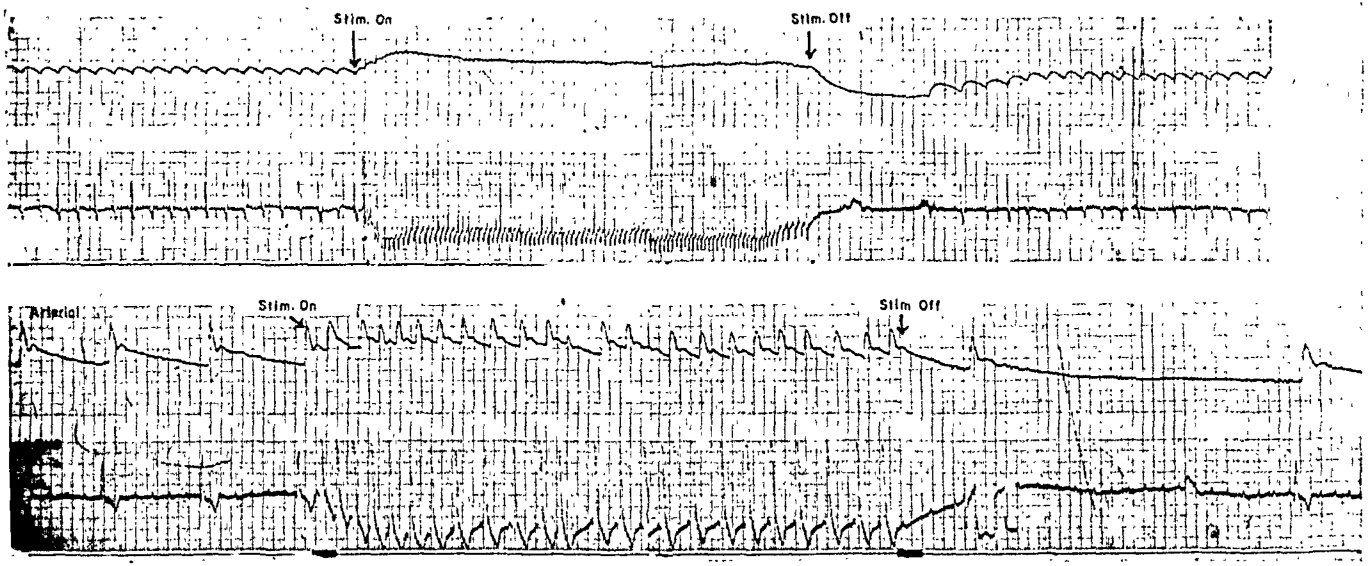

Fig. 2.—Two segments of a tracing showing the application and removal of the p-wave stimulator. The upper segment shows the mean arterial pressure rise with stimulation and the lower segment shows individual contractile pressure changes.

to the right auricle and near the apex of the ventricles. These wires were brought out of the chest cavity and the distal ends buried in the subcutaneous tissue.

Measurements of the arterial pressure, pulse rate, venous pressure, and tracings of the electrocardiogram and electroencephalogram were made pre- and postoperatively and were repeated when periods of stimulation were carried out. Cardiac outputs using the indigo carmine dye technique were done on some animals pre-block, post-block, and post-stimulation.

After a period of time elapsed to allow for healing from the operation, the leads were exposed under local anesthesia and p-wave stimulator attached. The animals could be stimulated for any length of time and, if desired, the leads put back in the subcutaneous tissue and the wound closed for later stimulation.

Fifty-nine animals had an attempt at destruction of the bundle of His. Thirty-nine of these animals developed a complete and permanent block and were available for subsequent stimulation.

RESULTS

Utilizing the group of animals previously described, approximately 400 hours of stimulation have been carried out. The duration of stimulation has varied on individual dogs from 30 minutes to 72 hours. Long-term stimulation has been possible with the production of a stable electrocardiogram and only minimal changes necessary in the settings of the stimulating mechanism.

Table I shows the average changes in pulse rate, peripheral arterial pressure, venous pressure, and cardiac output that occur prior to destruction of the bundle of His, after block and the development of an idioventricular rhythm, and during stimulation of the ventricle by the p-wave triggered stimulator.

TABLE I

	PREOP.	POST-BLOCK	STIMULATION
Average pulse rate per minute	126	62	126
Average arterial pressure (mm./Hg)	122/70	108/60	126/72
Average venous pressure	6	12	5
Average cardiac output Index $(l/M.^2)$	2.25	1.24	2.23

The marked decrease in pulse rate, average fall of 14 mm. Hg in systolic arterial pressure, 100 per cent increase in caval venous pressure, and 55 per cent reduction in cardiac output are obvious. During stimulation these values quickly revert to normal (± 5 per cent) (Fig. 2).

We feel the decreased cardiac output and increased venous pressure to be the most deleterious effects of the idioventricular rhythm. Mowlem and Campbell[7] have recently reported the acute changes occurring with induced heart block but found that changes affecting the left heart (left atrial pressure and left ventricular end-diastolic pressure) rather quickly reverted to normal. This rapid return to normal does not hold true in a chronic situation with respect to venous pressure and cardiac output. Sixty per cent of our animals which survived 3 months developed massive ascites and other evidence of right ventricular failure. These changes respond slowly to digitalis and paracentesis.

In attempts to evaluate the advantages of the p-wave stimulator we have studied cardiac outputs that could be obtained using conventional timed stimulators acting through a ventricular electrode. The results of these tests are presented in Table II. It seems that with persistence and frequent measurements of cardiac output that one might be able to arrive at a normal output with a mechanically timed stimulator. We were not, however, able to do this with any degree of accuracy. Certainly a return to essentially normal physiologic measurements is more quickly and easily made with the auricle triggering the stimulator.

TABLE II*

		PRE-BLOCK INDEX	BLOCK INDEX	STIMULATION INDEX
A. P-Wave Stimulator		2.94	1.47	2.92
B. Conventional Timed Stimulator				
Rate	*Voltage*			
48	8.2			1.15
90	8.6			2.74
144	8.6			3.0
152	9.0			3.47

*Cardiac indices are stated in liters per square meter of body surface.

DISCUSSION

This is a preliminary report on one of the approaches to extracardiac stimulation. We know of no other such unit available. Folkman and Watkins[8] have reported the use of a transistor unit to amplify the auricular p wave and use this to trigger the ventricle but this has certain disadvantages. Among these objections are the poor electrical characteristics of the p wave for stimulation, lack of a delay circuit (p-r interval), and long duration of the stimulus.

The unit described herein has proved to be simple to use and takes advantage, except for the muscle potential amplifier, of commercially available circuits. As the unit now stands it is bulky and not very mobile. These disadvantages can be obviated, however, by transistorizing the circuits and work along this line is progressing.

One problem which still must be answered is the duration of time one can stimulate through a single set of implanted electrodes. At the present time, 6 to 8 weeks of constant stimulation will cause enough fibrosis to prevent adequate stimulation. This period can be lengthened by intermittent stimulation. The solution to this problem must be reached, however, since, with direct electrodes, shocks in the range of 4 to 12 volts for stimulation are well tolerated by the heart and the remainder of the organism for long periods of time. If one relies on external cardiac pacemaking through the intact chest, voltages may go as high as 180 volts (Zoll, unpublished). Electric shock in this range is not only very uncomfortable for the patient but the individual also suffers the effects of a tonic seizure with each ventricular contraction.

SUMMARY

1 A p-wave triggered, ventricular, extracardiac stimulator has been described which experimentally produces physiologic hemodynamic changes

2 This unit has been evaluated on a large group of experimental animals and has proved safe and effective

3 The decreased cardiac output and the elevated venous pressure appear to be the most important functions to consider in treating temporary or permanent heart block

4 Some of the difficulties associated with extracardiac ventricular stimulation are discussed

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(For Discussion, see page 638)

"TRANQUILIZATION" OF THE HEART WITH THE ATARACTIC DRUGS

Russell M. Nelson, M.D., Ph.D., Salt Lake City, Utah

Cardiac arrhythmias continue to pose a hazard to patients subjected to cardiac surgery. The incidence has been lowered by an understanding of the importance of maintaining normal physiologic conditions, and yet there are many instances in which the pathologic anatomy to be corrected has set the stage for possible cardiac irregularities. Quinidine and Pronestyl, drugs widely used for the medical control of arrhythmias, have side effects which make their use undesirable before or during surgery. With the observation in our laboratory that certain antihistaminic and ataractic (tranquilizer) drugs apparently exert a stabilizing or "tranquilizing" effect on the heart,[1] and in view of reports in the literature suggesting clinical usefulness of certain ataractic drugs in cardiac arrhythmias,[2, 3, 4] this study was begun to see if the ataractic drugs could convert ventricular fibrillation into a normal sinus rhythm. Subsequently, questions were raised regarding the possible effects of these drugs on the normally beating heart, and if any protection might be afforded against the occurrence of ventricular fibrillation.

The study and the results reported here are regarded as preliminary observations of work in progress. Nonetheless, these findings appear to be of such interest that an initial report seems warranted.

METHOD

An isolated canine heart, biologically supported by a donor dog, was utilized as the preparation for study. The isolated heart was procured from a dog via a right thoracotomy under pentobarbital anesthesia. The heart was arrested by injecting 20 ml. potassium citrate (2.5 per cent) into the coronary arterial circulation after the dog had been heparinized (3 mg. per kilogram). After removal of the heart, the proximal end of the transected thoracic aorta was cannulated to permit retrograde perfusion of the coronary arteries. The brachiocephalic artery was cannulated to monitor the perfusion pressure and other aortic branches were ligated. Electrocardiographic tracings were recorded

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from surface electrodes, and the temperature was determined by a thermistor probe immersed in the blood after it had been ejected from the isolated heart into a receiving funnel.

The temperature was maintained at 85° to 98° F. by heat from infrared lamps adjacent to the isolated heart, and with a heating pad under the supporting dog.

Blood was delivered from the femoral artery of the supporting dog to the isolated heart via tubing placed through an occlusive Sigmamotor pump. Flow rates were then governed by adjusting the pump so that the pressure in the isolated heart preparation was within normal limits. Blood was then collected and returned to the femoral vein by gravity. Respirations of the supporting dog were maintained with oxygen administered by intermittent positive pressure via an endotracheal tube. Arterial pressure was continually monitored on an oscilloscope.

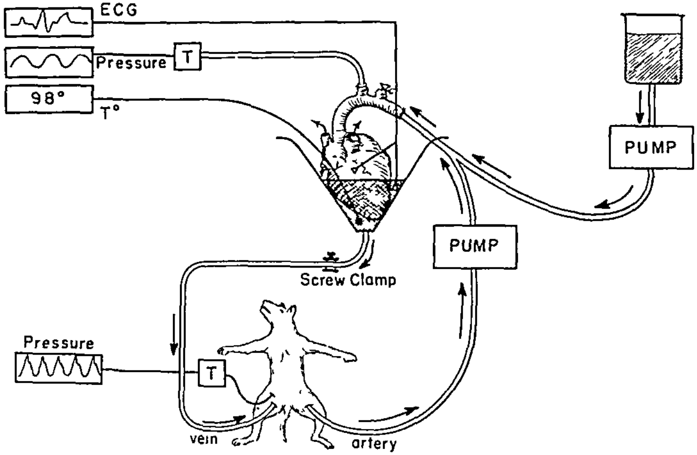

Fig. [illegible] *of the biologically supported isolated heart preparation.* Arte.. [illegible] log is pumped, in retrograde fashion, into the thoracic aorta. [illegible] art, blood is collected and returned to the dog via the femora[illegible] of the isolated heart electrocardiogram, pressure, and temperature, in addition to the pressure of the supporting dog, are depicted. Drugs to be assessed are added from a reservoir into the arterial line by another occlusive pump.

Drugs to be tested were added to the arterial limb of the circuit just proximal to the isolated heart by means of a second occlusive Sigmamotor pump, adjusted to deliver 100 to 125 ml. per minute.

Spontaneous cardiac activity in the isolated heart was usually established within an hour of elective cardiac arrest. The type of cardiac rhythm was controlled by means of electric shocks. If normal sinus rhythm was desired, one shock of 90 volts was used; if ventricular fibrillation was desired, repeated shocks

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TABLE I. ADMINISTRATION OF ATARACTIC DRUGS TO ISOLATED HEARTS IN VENTRICULAR FIBRILLATION

	CONVERSION VF* TO NSR†	DOSAGE REQUIRED (MG./MIN.)		DOG WEIGHTS (LB.)		SUBSEQUENT PROTECTION VS. V.F.*
				SUPPORTING DOG	HEART DOG	
Atarax	+	33	3	38	31	+
	+	750	80	75	38	+
	+	65	27	43	21	
	+	15	1	40	29	
	0	550	89	43	31	
	+	100	18	38	36	+
	0	250	25	38	32	
	0	300	66	40	23	
	+	50	7	50	20	
	+	115	14	52	27	
	+	100	14	45	26	
	+	40	3	48	24	+
	+	15	2	63	14	+
	+	25	5	42	18	+
	+	50	4	-	-	+
Compazine	+	45	4	32	24	+
	+	100	26	45	35	0
	0	200	56	53	33	0
	+	40	3	53	24	0
Phenergan	+	100	23	35	26	+
	+	65	32	49	26	
Serpasil	+	7.5	2	56	30	0
Sparine	+	100	35	39	25	+
Stelazine	+	40	3	49	22	
	+	25	2	54	30	+
	+	90	12	38	28	+
	+	33	1	46	20	+
	+	100	27	39	33	+
	+	25	2	39	33	+
	+	50	3	42	24	+
	+	30	2	38	31	
Thorazine	+	85	23	42	28	0
	+	100	31	47	27	0
Trilafon	0	100	5	38	31	
	+	65	47	31	29	0
	+	90	26	39	26	+
	+	300	45	38	29	0
	+	25	3	58	30	0
Quinidine	+	53	1	42	27	+
	+	28	1	67	34	+
	+	50	2	42	32	0
	+	110	31	47	31	0

*VF = Ventricular fibrillation.
†NSR = Normal sinus rhythm.

from one rhythm to the other. No apparent correlation was noted between the type of conversion and the other measured variables. Control perfusions of saline before and after the experimental drugs did not alter the pattern of fibrillation. Representative electrocardiographic tracings showing these results are portrayed in Fig. 2.

2. *Effects of Drugs on the Heart in Normal Sinus Rhythm.*—

The ataractic drugs and quinidine, under conditions of this experiment, produced bradycardia; and in the example illustrated, Stelazine (50 mg.)

of 3 volts were used. Duration of the shock was 0.1 second. Once reproducible responses were achieved, ventricular fibrillation was induced and the preparation was ready for study.

Five hundred milliliters of normal saline was first administered over a period of 4 to 5 minutes as a control. Then, by means of shocks of voltages as described, the heart was put into a normal sinus rhythm, then to ventricular fibrillation, repeating several times, again to ensure validity of the preparation. Ventricular fibrillation was then again induced. The drug to be tested was then added. For the ataractic drugs, the initial concentration was 50 mg. in 500 ml. saline (or the equivalent), or multiples thereof in case more drug was required. With quinidine, 80 mg. or multiples thereof were used. If the heart was still in fibrillation at the end of this infusion, additional mixtures were prepared and administered. When conversion from ventricular fibrillation to normal sinus rhythm had taken place, the volume given and the time for administration were noted.

Drug-induced protection against ventricular fibrillation was presumed to be present if the same stimuli, which repeatedly caused fibrillation previously, failed to do so after administration of a drug.

This report concerns forty-two experiments which were performed after the techniques and protocol were standardized. The following drugs have been studied: hydroxyzine (Atarax*) in 15 experiments, prochlorperazine (Compazine†) in 4, promethazine (Phenergan) in 2, reserpine (Serpasil) in 1, promazine (Sparine) in 1, trifluoperazine (Stelazine†) in 8, chlorpromazine (Thorazine†) in 2, perphenazine (Trilafon‡) in 5, and, for comparison, quinidine. (For the sake of simplicity the proprietary names of these agents are used rather than the generic names.)

RESULTS

1. *Effects of Drugs on the Heart in Ventricular Fibrillation.*—

Each of the ataractic drugs used proved to be capable of converting the heart in ventricular fibrillation to a normal sinus rhythm. Of the 38 hearts so tested, 33 were thus converted and 5 were not. The dosage required varied widely and did not correlate with any of the measured variables. In the remaining 4 dogs, quinidine similarly was effective in restoring a regular beat to the fibrillating heart and with a time-dosage range comparable to that of certain ataractic drugs.

The results are tabulated in Table I.

Two distinct types of electrocardiographic patterns were observed during the conversions. In some instances, the amplitude of the ventricular fibrillation became progressively lower until a state of asystole ensued. From asystole, recovery to normal sinus rhythm regularly followed. In other instances, the intermediary stage of asystole was not observed, there being a direct conversion produced asystole at the end of a 3-minute infusion. Subsequent recovery with a normal electrocardiogram is shown after cessation of the drug in Fig. 3.

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*Kindly supplied by J. B. Roerig & Company, New York, N. Y.

†Kindly supplied by Smith, Kline & French Laboratories, Philadelphia, Pa.

‡Kindly supplied by Schering Corporation, Bloomfield, N. J.

3. *Subsequent Protection Against the Artificially Induced Ventricular Fibrillation.—*

This was demonstrated in 17 of 26 instances in the tranquilizer groups, and in 2 of 4 trials in the quinidine group. This was not observed in 76 trials in the control group.

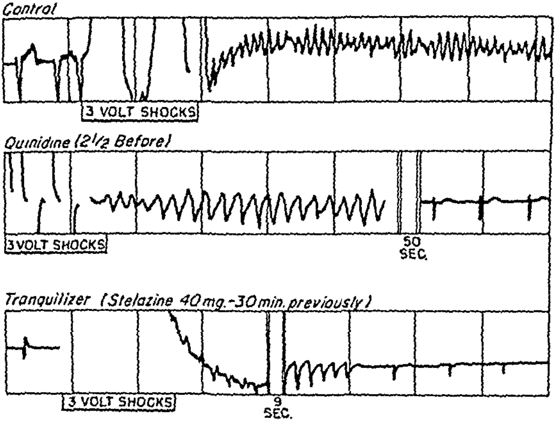

Fig. 4.—Drug-induced protection vs. low-voltage shock ventricular fibrillation. The first line shows the electrocardiographic tracing of a heart in normal sinus rhythm subjected to 3 volt shocks and the resulting pattern of ventricular fibrillation. Spontaneous reversal to normal sinus rhythm does not occur in several hours of follow-up.

The center tracing shows the residual protective effect of quinidine with "spontaneous" reversal to a normal rhythm within a minute of the low-voltage shocks.

The third tracing shows a similar protection afforded by Stelazine, which had been given 30 minutes prior to the administration of the low-voltage shock. Note the rapid return to a normal sinus rhythm.

Table II. Subsequent Protection Against Ventricular Fibrillation

	TRIALS	APPARENT PROTECTION	NO APPARENT PROTECTION
Saline	76	0	76
Ataractic drugs	26	17	9
Quinidine	4	2	2

The duration of this protection was variable but, on the average, lasted about 30 to 45 minutes. These results are included in the last column of Table I. Illustrations of representative electrocardiographic tracings are reproduced in Fig. 4.

DISCUSSION

As indicated in earlier remarks, this represents a preliminary report of exploratory work currently in progress. There is much more to assess before the possible application of this information is indicated. Nevertheless, with the

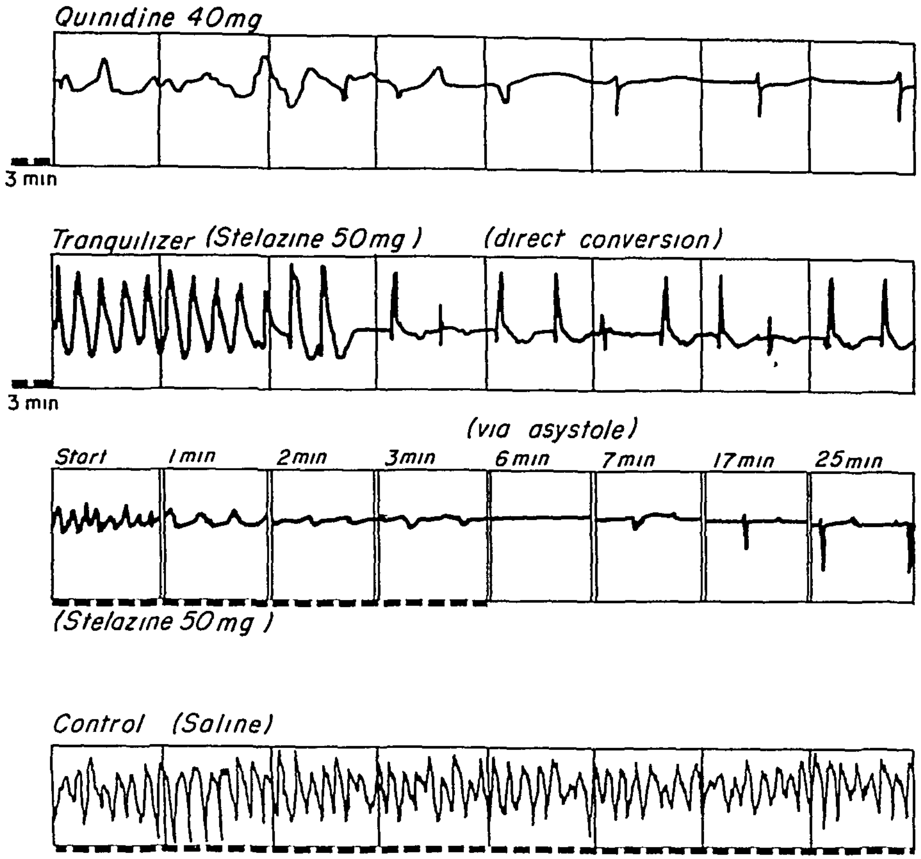

Fig. 2.—Ventricular Fibrillation. Illustrative electrocardiographic tracings are reproduced here to show the direct conversion to a normal sinus rhythm 3 minutes after the administration of quinidine or Stelazine. The third line shows the intermediary state of cardiac asystole. Typical saline control tracing is shown for comparison. Time lines are at 1-second intervals. Paper speed in recorder is 25 mm. per second. The interrupted heavy line denotes time of continuous drug administration.

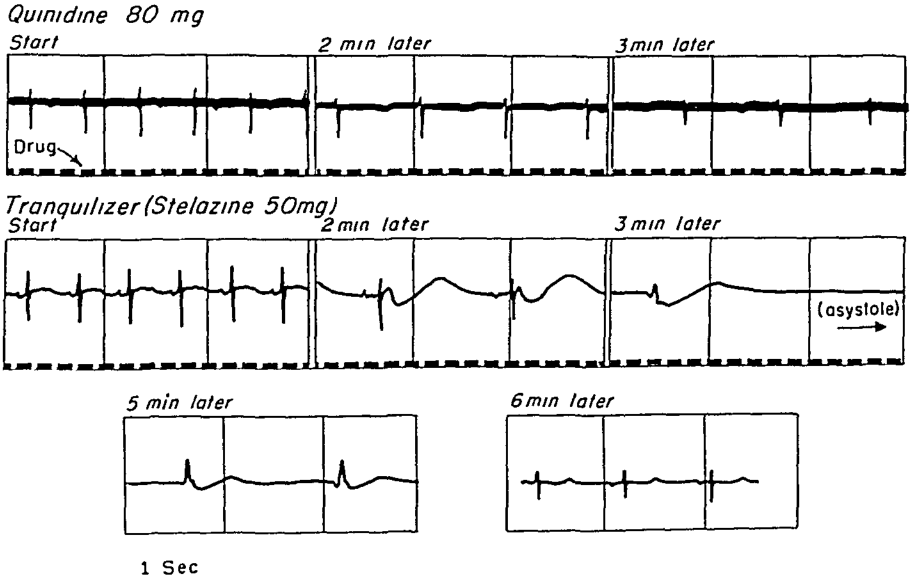

Fig. 3.—Normal Sinus Rhythm. This figure illustrates the bradycardia that is associated with the administration of quinidine or a tranquilizer to the heart in normal sinus rhythm. In the second instance, cardiac asystole resulted with return of normal electrocardiogram after cessation of the drug.

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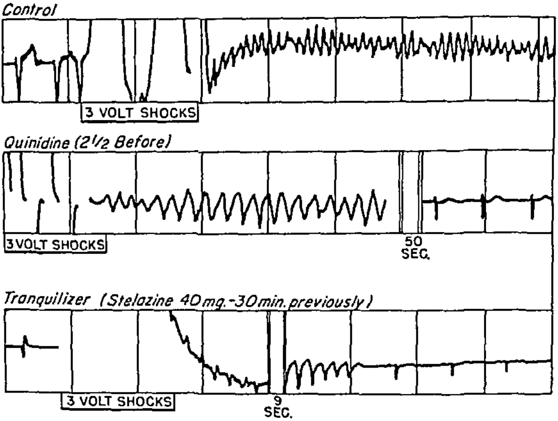

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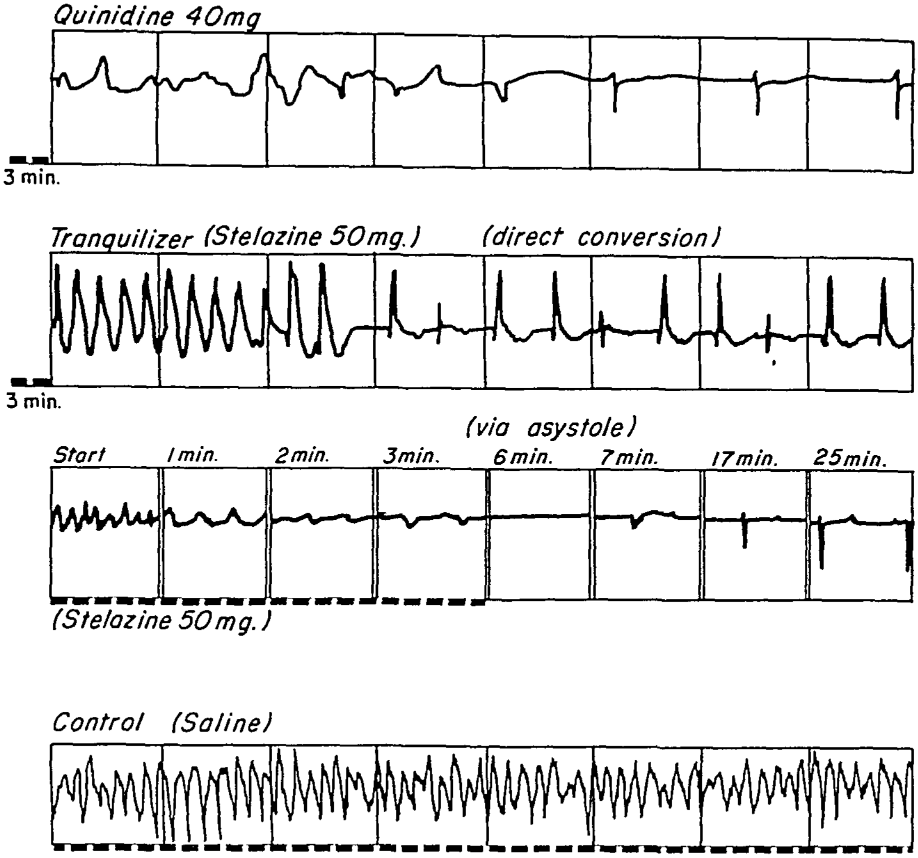

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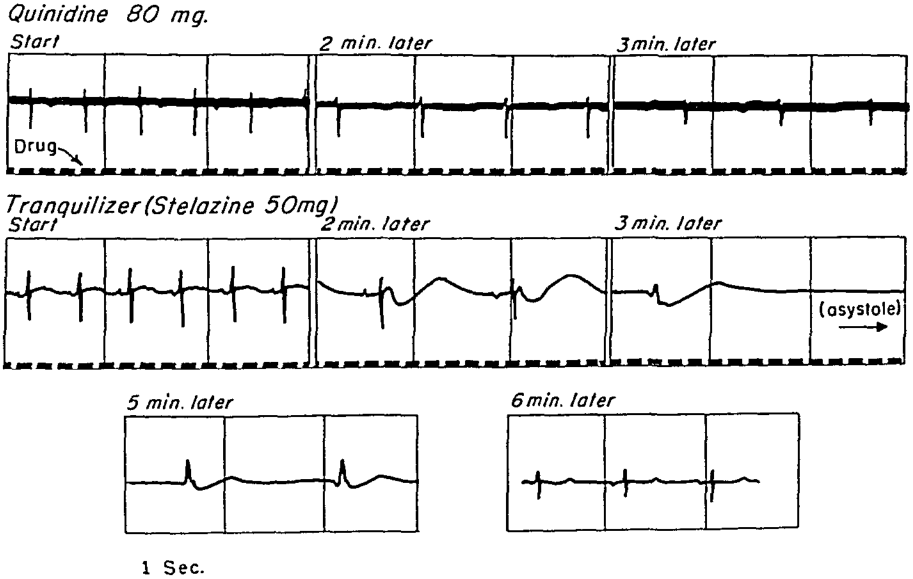

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The author is deeply grateful to Mr. James W. Henry, Mr. C. Gordon Frank, Mr. Dennis W. Christensen, Mr. David R. Haymond, Mr. John M. Peters, and Mr. Carl R. Peterson for their work and loyal assistance in this study. For review of the manuscript, gratitude and thanks are extended to Dr. Hans H. Hecht, Professor of Medicine (Cardiology), and Dr. Walter J. Burdette, Professor of Surgery, University of Utah College of Medicine.

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(For Discussion, see page 638.)

widespread use of the ataractic or tranquilizer drugs, and with the apparent low incidence of side effects or complications, the possible clinical usefulness of these agents in preparing a patient for cardiac surgery immediately becomes apparent. A case in point is that of V. B. L., aged 10, a patient with a large ventricular septal defect and pulmonary hypertension (PA pressure 90/40). On each physical examination in the period of preoperative evaluation, the rhythm of his heart was characterized by frequent premature ventricular contractions. Because this had been noted without exception by several examiners over a period of 3 months, and a tracing again confirmed frequent ventricular extrasystoles, he was given a small dose of an oral tranquilizer and a repeat electrocardiogram was taken 24 hours after the previous one. No irregularities were observed on the oscilloscope in 1 hour of observation. The electrocardiograms are reproduced in Fig. 5. This patient subsequently underwent open heart surgery for repair of the ventricular septal defect and has made an uneventful recovery. Other clinical experience is similarly suggestive of beneficial effects, but lack of precise controls makes interpretation and evaluation difficult.

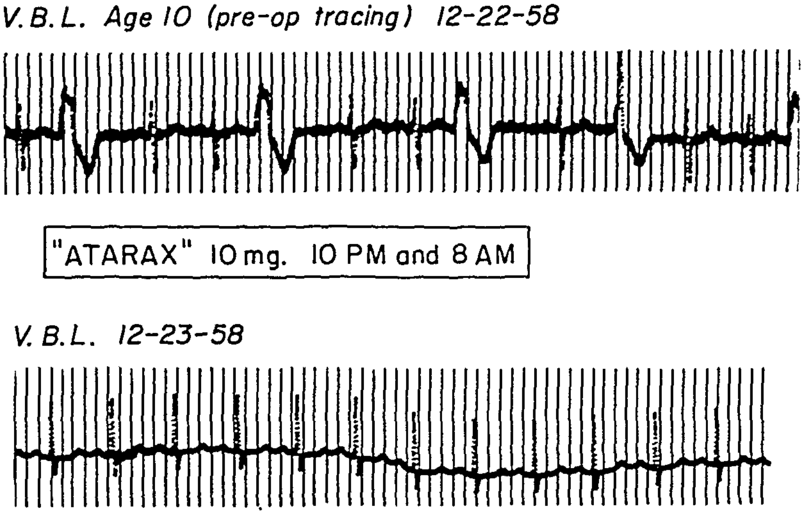
V.B.L. Age 10 (pre-op tracing) 12-22-58
"ATARAX" 10 mg. 10 PM and 8 AM
V.B.L. 12-23-58

Fig. 5.—Ventricular Septal Defect With Pulmonary Hypertension. Note the disappearance of the frequent premature ventricular contractions after small doses of a tranquilizer agent.

It is interesting to postulate that the hypotension which occasionally follows the use of these drugs may, in some cases, be due to a direct cardiac effect.

CONCLUSIONS

1. Under conditions of these experiments, employing the biologically supported isolated canine heart preparation, infusion of an ataractic drug into the coronary circulation is capable of converting ventricular fibrillation into a normal sinus rhythm.

2. In the majority of instances, residual protection follows the administration of an ataractic drug against the artificial production of ventricular fibrillation by repeated low-voltage shocks.

3. These drugs are quite similar to quinidine in the direct effect on the rhythm of the canine heart.

This has allowed us to determine the serum potassium level which must be reached within a certain time in order to produce these phenomena.

Having established the fibrillating and arrest doses of potassium, we have then investigated the ionic changes which result from various factors operating singly or in combination during surgical procedures. These include: anoxia, stress, hemorrhage, hypercarbia, and drugs.

METHODS

Healthy, normal dogs under Nembutal anesthesia have been used for the studies. Following intubation with a cuffed endotracheal tube, all animals have been heparinized with 1 mg. per kilogram to prevent clotting during collection of multiple blood specimens. Femoral artery pressure was measured directly on a Sanborn Twin-Viso Recorder by means of a pressure transducer. Lead II electrocardiograms were monitored continuously during most of the procedures. Potassium chloride solution was prepared with a concentration of 100 mg. per cubic centimeter and diluted with sterile water to the proper volume for injection. All KCl and drugs were injected very rapidly through a No. 16 catheter in the opposite femoral vein. Blood samples were withdrawn with a large caliber needle from the carotid artery, or were bled off directly from this source.

RESULTS IN THE VARIOUS SERIES

Effect of Potassium Injection.—

Sixty dogs were injected witih varying amounts of potassium chloride. These injections were given very rapidly, usually within 2 to 4 seconds. Blood specimens were taken every *10 seconds* for determination of serum potassium levels.

Fig. 1, *B*, summarizes the results of this work. Ninety per cent of the animals which received 20 mg./Kg. went into ventricular fibrillation. One dog did not show fibrillation. This amount apparently represents the "fibrillating dose" of potassium. Less than this causes either no fibrillation (10 mg./Kg.) or only a small incidence (15 mg./Kg.). At the 50 and 60 mg./Kg. level, 40 to 60 per cent of the animals showed ventricular fibrillation, and the rest went into cardiac arrest. Cardiac arrest resulted at the 70 mg./Kg. level, without ventricular fibrillation in every case.

Fig. 1, *A*, shows the mean serum potassium response of all dogs which received 15 mg./Kg. and 20 mg./Kg. All animals which had a potassium rise of 200 per cent or more above their base level within 10 seconds following injection went into ventricular fibrillation. Dogs with peak potassium values of less than 200 per cent within 10 seconds recovered and did not fibrillate.

Fig. 2 presents the data on the 15 mg./Kg. and 20 mg./Kg. series. These data substantiate the time-dose relationship between potassium and ventricular fibrillation. Here, again, the first injections which resulted in elevation of serum potassium level to 200 per cent or more above the base level caused ventricular fibrillation. The animals which did not fibrillate received a second

THE MECHANISM OF VENTRICULAR FIBRILLATION AND CARDIAC ARREST DURING SURGERY

Archer S. Gordon, M.D., Ph.D. (by invitation), and*
John C. Jones, M.D., Los Angeles, Calif.

INTRODUCTION

The best approach to the problem of ventricular fibrillation and cardiac arrest is prevention. This implies an understanding of the mechanisms underlying their production. Many factors have been incriminated as the basis for these phenomena. However, their proof requires a technique for producing ventricular fibrillation and cardiac arrest under controlled experimental conditions in which each factor or combinations of factors can be evaluated.

In studies of the phenomena attending drowning in various species we have noted, as have others, that some animals succumb to ventricular fibrillation, whereas others die from cardiac arrest. Careful tests indicate that the former results from extreme ionic imbalances due primarily to rapid and explosive shifts in potassium. The cardiac arrests are almost exclusively the result of anoxia without serious ionic imbalances.[1]

It would appear that factors producing anoxia and ionic shifts might well be responsible for the occurrence of ventricular fibrillation and cardiac arrest during surgery. This study was undertaken to investigate this premise.

EXPERIMENTAL DESIGN

It is known that rapid injections of various ions can produce ventricular fibrillation.[2] We have seen this result from potassium, calcium, and magnesium, and are assured that it may happen with other substances. However, in human and animal systems, the only ion which can be mobilized from its depots and translocated through the body rapidly enough and in large enough amounts to produce sudden severe cardiac arrhythmias and ventricular fibrillation is potassium.[3, 4]

Therefore, we have used potassium chloride in graded doses to induce cardiac arrest and ventricular fibrillation and study the time-dose relationship.

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Fig. 2 reveals an interesting observation in the 20 mg./Kg. series. When the potassium peak was 200 per cent but was reached *in 20 seconds instead of* 10 seconds, ventricular fibrillation did not result. The time-dose-response relationship here is such that a specific dose must be injected within a specific time and result in a specific potassium rise within a specific period. These studies indicate that to produce vetricular fibrillation, 15 mg./Kg. must be injected intravenously within 2 to 4 seconds and cause a 200 per cent elevation in serum potassium level above the base line within 10 seconds following injection. The animal cited in the 20 mg./Kg. series probably did not fibrillate because the injection took longer than 4 seconds. We have noted several times that doses of KCl, which usually produced fibrillation when injected within 4 seconds, failed to do so when the injection took 5 or more seconds. Another observation to substantiate this is that amounts of potassium as large as 300 mg./Kg. injected over a period of 1 minute did not cause ventricular fibrillation or cardiac arrest.

In those dogs in which large doses of potassium produced arrest, the peak serum level showed a rise of between 600 and 1,000 per cent. All of the 70 mg./Kg. animals showed such responses. However, in the 50 mg./Kg. and 60 mg./Kg. series no specific relationship could be found between per cent elevation of serum potassium and incidence of ventricular fibrillation or cardiac arrest.

Serum sodium levels showed no significant change in these animals.

Effect of Anoxia.—

Having established the serum potassium level and timing required to produce ventricular fibrillation, we next evaluated various factors which might be operative during surgery and which could reproduce these phenomena under clinically simulated conditions. These factors included anoxia,[5, 6] stress,[7, 8] hemorrhage,[3, 4] hypercarbia,[9-12] and drugs.[13]

Acute anoxia was produced in 9 dogs by tracheal clamping. They showed a mean potassium rise of 51 per cent within 5 minute. Ventricular fibrillation did not occur. They all progressed to bradycardia and ultimately to cardiac arrest. These results are summarized in Fig. 3.

Chronic anoxia was studied in 7 dogs which rebreathed into a bag through a soda lime cannister to prevent carbon dioxide accumulation. Within 10 minutes their mean potassium level had risen to 53 per cent. One animal went into cardiac arrest at 8 minutes with a 16 per cent potassium rise. The others experienced bradycardia and cardiac arrest. One animal went from cardiac arrest into ventricular fibrillation after 12 minutes of anoxia. This ventricular fibrillation represents a terminal cardiovascular phenomenon common to dying hearts rather than the cause of death.

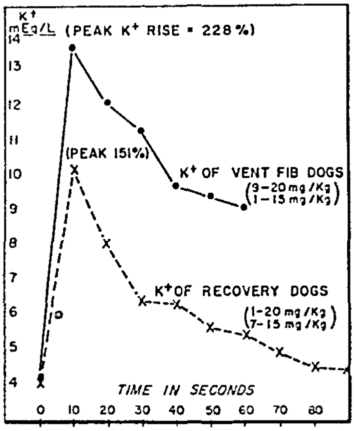
These results indicate that "pure" anoxia results in cardiac arrest and is seldom, if ever, a cause of ventricular fibrillation.

Effect of Epinephrine.—

To simulate severe stress, intravenous epinephrine was administered to 72 dogs. The first 11 animals were injected with 0.05 mg./Kg. The serum potassium level began to rise significantly at 30 seconds and reached a peak of 88 injection of the same amount 30 minutes later. All animals with potassium elevations of 200 per cent, resulting from the second injection, experienced ventricular fibrillation.

Potassium Injection Series

A. Mean Serum K+ Response In All Dogs Receiving 15 mg KCl/Kg and 20 mg KCl/Kg



B. Response of All Dogs To Potassium Injection

KCL DOSE	No DOGS	VENT FIB	CARDIAC ARREST	RECOVERY
10 mg	10	0	0	100 %
15 mg	10	30 %	0	70 %
20 mg	10	90 %	0	10 %
40 mg	4	100 %	0	0
50 mg	13	60 %	40 %	0
60 mg	9	45 %	55 %	0
70 mg	5	0	100 %	0

Fig. 1.

Potassium Injection Series

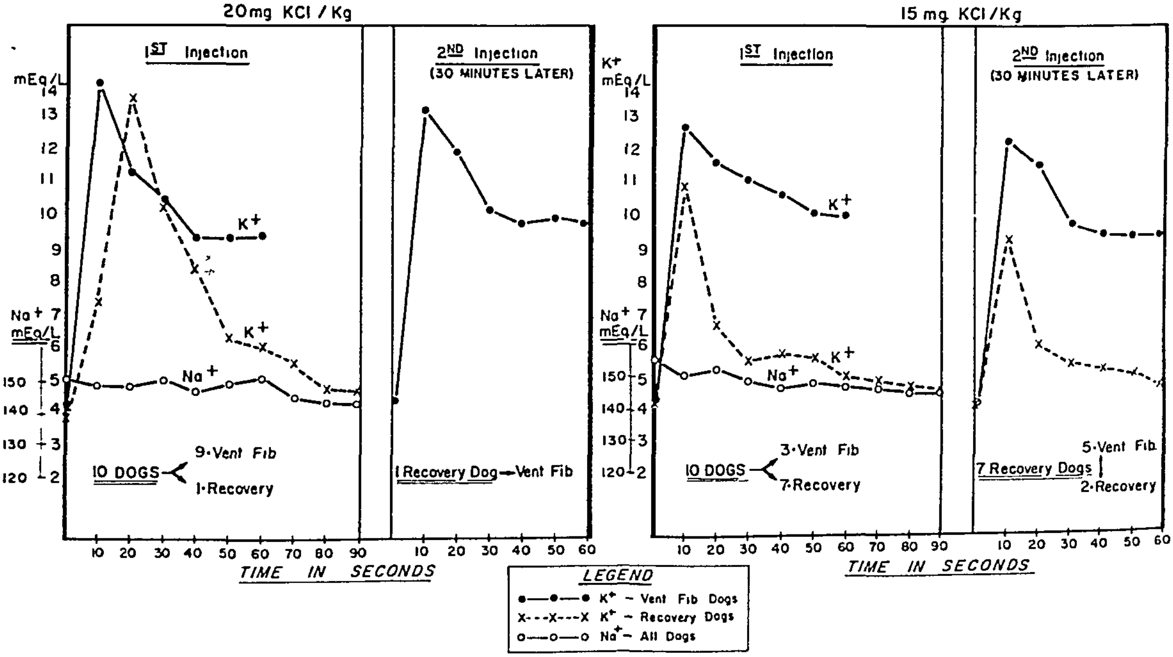


Fig. 2.

To determine whether a series of stresses in close succession might produce a cumulative response with respect to potassium elevation, a series of dogs received two injections of 0.05 mg./Kg. each, separated by intervals of 15, 30, or 60 seconds. The results recorded in Table I indicate that these dogs had essentially the same response as the animals which received only a single injection.

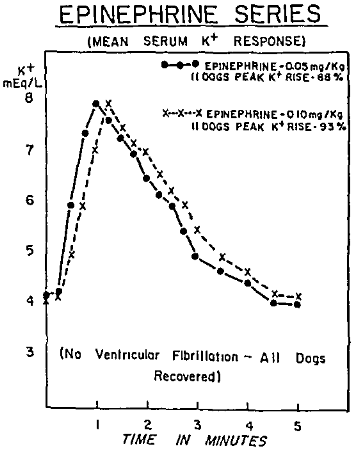


Fig. 3*B*.

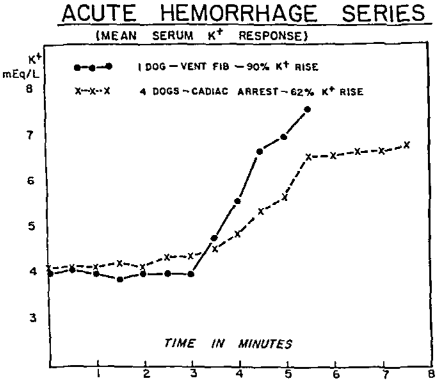


Fig. 3*C*.

To determine the effect of stress produced at intervals of 10, 20, or 30 minutes, 12 dogs in each of 3 series received two doses of either 0.05 mg./Kg. or 0.10 mg./Kg. at these time intervals. As indicated in Table I, all animals per cent above the base level within 1 minute. No dog experienced ventricular fibrillation; the serum potassium level returned to normal in 4 to 5 minutes and all dogs recovered.

To determine if this was a maximum response, twice as much epinephrine (0.10 mg./Kg.) was administered to another series of 11 dogs. These animals showed exactly the same response. Epinephrine produced no change in the serum sodium level in any of these animals. These results are detailed in Fig. 3.

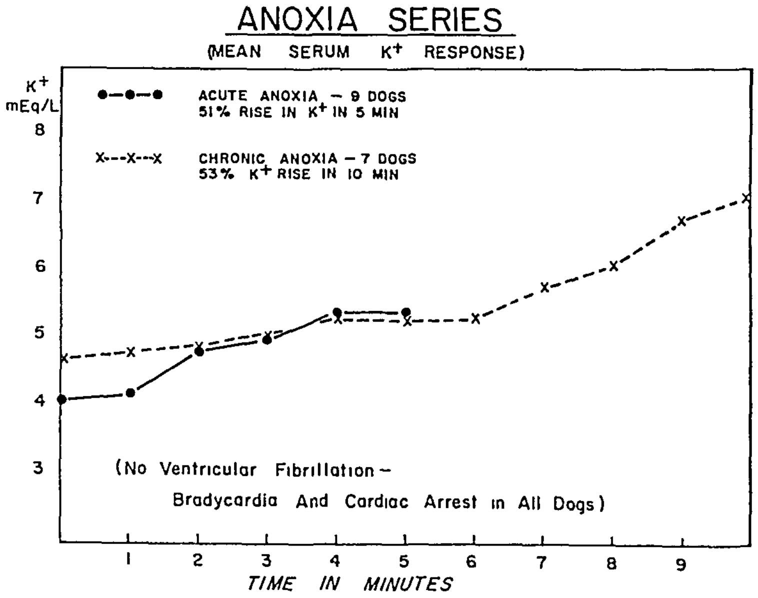


Fig. 3A.

TABLE I. INTRAVENOUS EPINEPHRINE SERIES

ADMINISTRATION	NUMBER DOGS	PEAK K+ RISE IN PER CENT*	
		0.05 MG./KG.	0.10 MG./KG.
A. *Single Dose Series*	11	88	
	11		93
B. *Summation Series*			
(Two doses each)			
1. 15 seconds apart	6	90	
2. 30 seconds apart	4	84	
3. 60 seconds apart	4	105	
C. *Repeat Dose Series*			
(Two doses each)			
1. 10 minutes apart	12		
1st dose		84	86
2nd dose		80	78
2. 20 minutes apart	12		
1st dose		82	84
2nd dose		73	80
3. 30 minutes apart	12		
1st dose		89	84
2nd dose		83	80

*In all series (1) the serum potassium rise started within 30 seconds following the injection, (2) the peak potassium level was attained in 60 to 90 seconds after injection, except B-2 (105 seconds) and B-3 (120 seconds), and (3) the serum potassium level returned to the initial level within 4 to 5 minutes, except B-2 (6 minutes) and B-3 (8 minutes).

To determine whether a series of stresses in close succession might produce a cumulative response with respect to potassium elevation, a series of dogs received two injections of 0.05 mg./Kg. each, separated by intervals of 15, 30, or 60 seconds. The results recorded in Table I indicate that these dogs had essentially the same response as the animals which received only a single injection

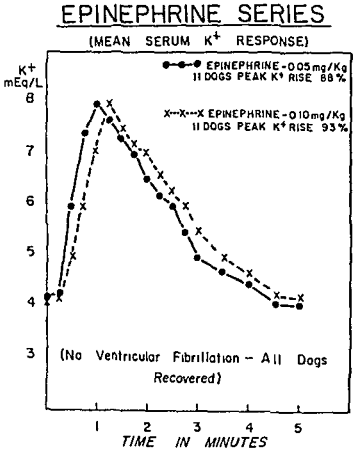


Fig. 3B

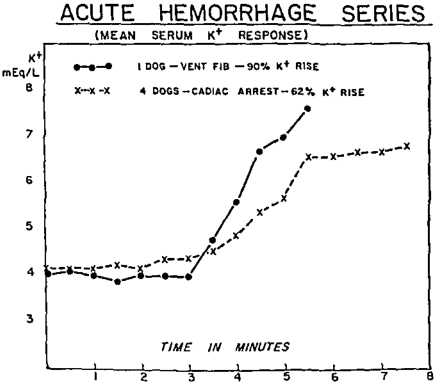


Fig. 3C.

To determine the effect of stress produced at intervals of 10, 20, or 30 minutes, 12 dogs in each of 3 series received two doses of either 0 05 mg /Kg. or 0 10 mg /Kg at these time intervals As indicated in Table I, all animals showed the same peak potassium rise as the animals which received a single injection. The only consistent difference was that the second dose always elicited a slightly diminished rise in potassium.

In all animals, the serum potassium rise started within 30 seconds following the injection; the peak potassium level was usually attained in 60 to 90 seconds after injection, and the serum potassium level returned to normal values within 4 to 5 minutes.

Severe stress (epinephrine) alone did not result in ventricular fibrillation in any animal.

Effect of Hemorrhage.—

Another important factor which may cause elevation of serum potassium during surgery is acute hemorrhage. This was evaluated in 5 dogs by withdrawing 50 c.c. of blood every 30 seconds. After 3 minutes, these animals showed a significant rise in serum potassium level. One animal fibrillated at 5 minutes with a serum potassium rise of 62 per cent. The other 4 animals showed a serum potassium plateau at about this same level and then rose to a peak potassium of 90 per cent above normal between 7 and 8 minutes, when they expired from cardiac arrest due to exsanguination. Fig. 3 summarizes these findings.

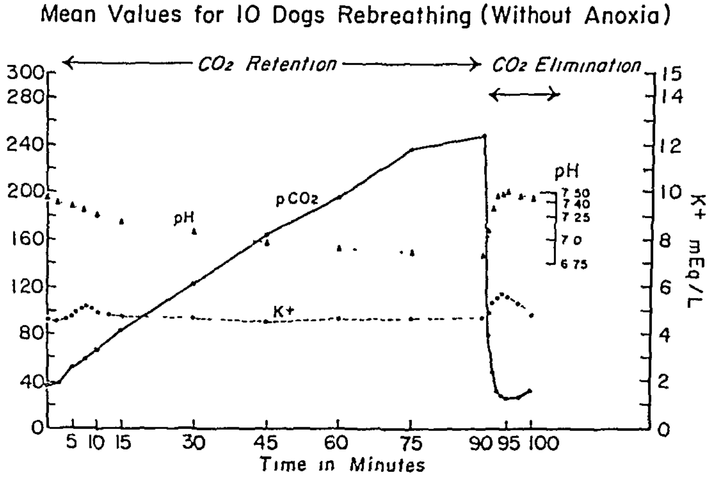

Mean Values for 10 Dogs Rebreathing (Without Anoxia)

Fig. 1.

Effect of Hypercarbia.—

Hypercarbia, independent of anoxia, was investigated by having 10 dogs rebreathe continuously for 90 minutes into a large rubber bag. Anoxia was prevented by replacing the oxygen as utilized. At the end of this time the bag was removed and the animals were subjected to hyperventilation with room air for 1 minute and then allowed to breathe spontaneously. After an initial transient rise the serum potassium level remained constant throughout the period of CO_2 retention. The pCO_2 climbed from 40 to 240 during this time. At the time of rapid CO_2 elimination, the pCO_2 dropped precipitously to subnormal levels during 2 to 3 minutes. Simultaneously the potassium level rose 24 per cent above the base level. Cardiac arrhythmias occurred in every dog at the time of CO_2 reversal. Nine of the dogs recovered but one progressed from ventricular tachycardia into ventricular fibrillation 4 minutes after the hyperventilation. Fig 4 illustrates these results.

Effect of Drugs.—

Numerous anesthetic agents and drugs are known to have sensitizing, excitatory, depressant, and other effects on the heart. It was not within the scope of this paper to investigate these thoroughly. However, a well known combination was used to demonstrate drug effect on serum levels. After preliminary sedation with Nembutal, 7 dogs were anesthetized with chloroform. When they were in stage III anesthesia, specimens of blood were drawn during a fifteen minute control period for determination of serum levels of calcium, sodium, potassium, magnesium, and chloride.

Then a rapid intravenous injection of 0.05 mg/Kg of epinephrine was made. Blood was drawn every 15 seconds thereafter for 2 minutes and then every ½ minute for 3 additional minutes. The findings are summarized in

Ionic Response to Epinephrine During Chloroform Anesthesia

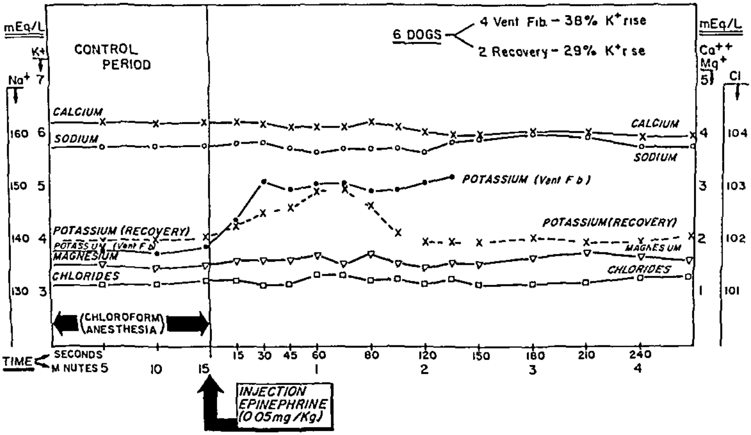


Fig 5

Fig 5. None of the ions showed any significant change except the potassium. Four of the dogs went into ventricular fibrillation with a serum potassium rise of 36 per cent. Two others had a peak potassium level of 25 per cent and recovered without fibrillating. One of the dogs received an overdosage of the anesthetic agent prior to the administration of epinephrine and died an anoxic death with cardiac arrest from the myocardial depression, as would be expected.

Effect of Summation of Factors.—

In the previous studies, great care was taken to evaluate the effects of single uncomplicated factors and situations. Such pure situations may occur clinically, but they are not the rule. They are essential in establishing base-level effects, but should be supplemented by studies of combinations of factors as might be anticipated on a practical basis. Accordingly, the effects of anoxia in combination with other factors were studied. The results in 65 dogs are summarized in Table II.

TABLE II. SYNERGISM OF FACTORS SERIES

FACTORS	NO. DOGS	RESPONSE: VENTRICULAR FIBRILLATION INCIDENCE (%)	RESPONSE: VENTRICULAR FIBRILLATION PEAK K^+ RISE (%)	RESPONSE: CARDIAC ARREST INCIDENCE (%)	RESPONSE: CARDIAC ARREST PEAK K^+ RISE (%)
A. Acute anoxia (4 min.) plus I.V. KCl					
(1) 10 mg./Kg.	12	50	239	25	187
(2) 15 mg./Kg.	12	50	278	42	198
B. Chronic anoxia plus CO_2 retention	9	0	—	100	85
C. Acute anoxia plus simultaneous epinephrine*	4	50	120	50	80
D. Chronic anoxia plus CO_2 retention plus epinephrine*	4	25	50	75	116
E. Epinephrine* 30 sec. before acute anoxia	4	50	89	50	81
F. Epinephrine* 60 sec. before acute anoxia	4	75	86	25	86
G. Epinephrine* 120 sec. before acute anoxia	4	50	100	50	88
H. Epinephrine* 30 sec. after acute anoxia	4	25	84	75	135
I. Epinephrine* 60 sec. after acute anoxia	4	25	106	75	93
J. Epinephrine* 120 sec. after acute anoxia	4	50	92	50	81

*Epinephrine (0.05 mg./Kg.), when used.

In two series of 12 dogs each, after 3 minutes of acute anoxia, 10 mg./Kg. or 15 mg./Kg. of potassium chloride was administered intravenously and the anoxia was prolonged to 4 minutes (Table II, *A*). In each of these groups, 50 per cent of the animals fibrillated. Twenty-five and 42 per cent of the rest went into cardiac arrest and the remainder recovered. In the 10 mg./Kg. series this represents a 50 per cent increase in ventricular fibrillation and a 75 per cent increase in mortality. In the 15 mg./Kg. group this represents a 20 per cent increase in ventricular fibrillation and a 60 per cent increase in mortality. Furthermore, the peak serum potassium levels in both fibrillating and nonfibrillating animals are higher than those produced by the drug alone. This indicates the potentiality for summation of responses when multiple factors are operating.

A series of dogs with anoxia plus hypercarbia and/or stress (Table II, *B-J*) provided two important observations: (1) in every instance (except chronic anoxia plus CO_2 retention) factors which did not produce ventricular fibrillation when operating singly, resulted in a 25 to 75 per cent incidence of fibrillation when they operated in combination, and (2) in every instance in which ventricular fibrillation occurred, the peak potassium level was only one half or less than the 200 per cent rise required to produce ventricular fibrillation with potassium chloride injections alone This indicates that ventricular fibrillation can occur even without summation sufficient to raise the potassium to fibrillating levels Apparently this is due to the synergistic effects of the factors An attempt to determine the most effective synergistic sequence was not too conclusive, but a slightly greater fibrillatory effect from stress preceding anoxia was indicated

Hypercarbia and chronic anoxia are both depressant Although this combination elevated the serum potassium level, cardiac arrest occurred without ventricular fibrillation In all other instances in which ventricular fibrillation did not occur, the anoxia was maintained until cardiac arrest occurred

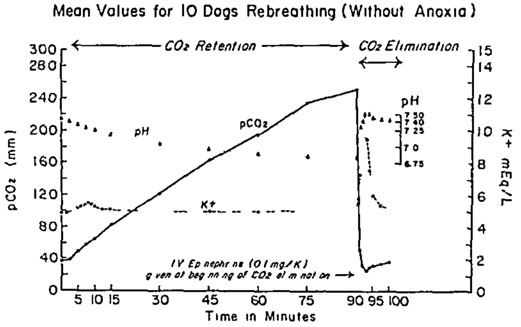


Fig 6

Fig 6 presents the summation resulting from rapid reversal of severe hypercarbia simultaneously with stress (I V epinephrine) This combination of factors resulted in an 88 per cent rise in serum potassium

The electrocardiograms showed more severe changes in this second group than in the preceding group of rapid reversal of hypercarbia Nine of the 10 dogs developed ventricular tachycardia, 1 of which progressed into ventricular fibrillation This animal had a 171 per cent rise in serum potassium

COMMENTS AND SUMMARY

Two hundred and forty six dogs have been studied in this survey of the mechanisms underlying ventricular fibrillation and cardiac arrest during surgery Results indicate that cardiac arrest is primarily a manifestation of anoxia and the most ominous sign of impending disaster is bradycardia On the other hand, ventricular fibrillation results from profound and sudden ionic imbalances Experimentally such imbalances can be produced by a variety of substances, but clinically only potassium is capable of being mobilized with the clinically, but they are not the rule. They are essential in establishing base-level effects, but should be supplemented by studies of combinations of factors as might be anticipated on a practical basis. Accordingly, the effects of anoxia in combination with other factors were studied. The results in 65 dogs are summarized in Table II.

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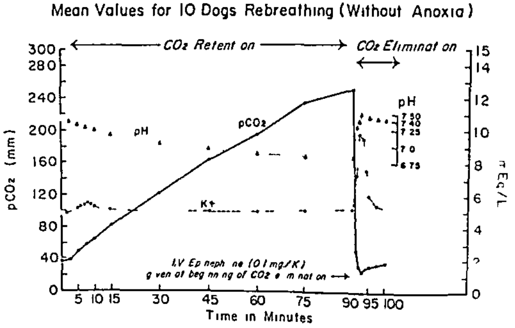

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Careful studies by Houssay and collaborators[3, 4] have revealed that the source of these potassium discharges is the liver. As a result of such noxious stimuli as anoxia, stress, reflex responses, hemorrhage, excitation, among others, the sympathetic nervous system and/or the adrenals act through nervous pathways to liberate the potassium-hexose-phosphate complex from the liver. Usually this is an efficient defense system of the body since the glucose provides energy and the potassium augments myoneural discharge in these emergencies.

However, if these act very rapidly, they result in a sudden shift of potassium into the blood stream and directly to the heart. The sudden appearance of large concentrations of potassium in the extracellular compartment results in large differences in electrical potential across the myocardial cell membrane. At low concentrations, little effect occurs except on the rate and rhythm of the heart. At higher concentrations (i.e., 20 mg./Kg.) local areas are triggered by differences in potential and ventricular fibrillation results. At very high concentrations, it appears that the myocardium is suddenly depolarized and overwhelmed into arrest by the massive transfer of ions.

The serum potassium level rapidly returns to normal levels because this ion is quickly translocated into muscle and body tissues. It is then gradually transferred back to its storehouse in the liver.

It has been shown here that various factors stimulating the release of potassium can act simultaneously or in sequence to produce summation. Of even greater significance is the fact that some of these factors and drugs and anesthetic agents act to sensitize, stimulate, irritate, or depress the myocardium. This provides further synergism.

An evaluation of the use of drugs or other ions to prevent or counteract the effects of anoxia and/or ionic imbalances is outside the realm of this paper. Preliminary studies on a series of 10 dogs have indicated that atropine is only slightly protective against the fibrillatory effect of 20 mg./Kg. of potassium chloride. In another series of 10 dogs, acetylcholine appeared to be somewhat more protective against the effects of 15 and 20 mg./Kg. of KCl.

However, this approach to the problem begs the basic issue regarding the cause of ventricular fibrillation and cardiac arrest during surgery. If anoxia, stress, hemorrhage, hypercarbia, and drug stimulation and depression underly the mechanism for these complications, the elimination or control of these factors provide the best means of preventing ventricular fibrillation and cardiac arrest.

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(For Discussion, see page 638.)

PREVENTION OF POSTHYPERCAPNEIC VENTRICULAR FIBRILLATION IN DOGS

Bernard Goott, M.D. (by invitation), and Fletcher A. Miller, M.D. (by invitation), Minneapolis, Minn.

VENTRICULAR fibrillation can be consistently produced in dogs, if, following prolonged hypercapnia, their arterial blood pH is rapidly raised to normal by ventilation with room air.[1] This procedure offers a consistent and reproducible method of studying the metabolic alterations which might be of influence in the production of ventricular fibrillation.

Inhalation of high concentrations of carbon dioxide results in a rise in the levels of potassium, inorganic phosphorus and glucose, with a simultaneous drop in the ionized calcium level. The ratio of ionized calcium to potassium shows a further decrease in the immediate posthypercapneic period when concurrent with the return to more nearly normal blood pH levels there is a sudden elevation of the serum potassium and a simultaneous drop in the ionized calcium.[2] In all likelihood, these values are indicative of an acute ionic alteration in the myocardium.

According to Tenney,[3] carbon dioxide inhalation serves as a potent stimulus to the sympatho-adrenal system. The circulatory changes and the metabolic alterations of hyperkalemia, hyperphospheremia, and hyperglycemia described above are all consistent with increased sympatho-adrenal activity.

In order to explore the possibility that these metabolic changes may be important in the precipitation of this type of fibrillation, the following investigations were undertaken.

A. *Sympatho-Adrenal Influence.*—To examine the influence of the cardiac sympathetic nerves an attempt was made to denervate the heart by means of bilateral sympathectomy. In a second series, Dibenzyline was given in an attempt to suppress the sympatho-adrenal response.

B. *Ionic Balance.*—The significance of the changes in ion concentrations was investigated as follows: (1) calcium gluconate was administered to a series of 12 dogs while inhaling the carbon dioxide mixture, and also in the immediate

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posthypercapneic period, (2) a second series of animals received magnesium sulfate, and (3) in another series, we attempted to suppress the rise in serum potassium by the use of insulin or corticoid preparations.

C. *The Effect of Quinidine Was Also Examined.*

METHODS

Healthy mongrel dogs weighing between 16 and 20 kilograms were used. Each animal was lightly anesthetized with sodium Pentothal, 10 mg./Kg., in order to perform the minor surgical procedures of femoral artery cannulation and tracheotomy. On recovery of the major reflexes, a mixture of 30 per cent CO_2/70 per cent O_2 was administered via the tracheotomy for a period of 2 hours, followed by a mixture of 40 per cent CO_2/60 per cent O_2 for a second 2-hour period. The dogs were next rapidly hyperventilated with room air using a mechanical respirator with an inspiratory pressure of 20 mm. Hg.

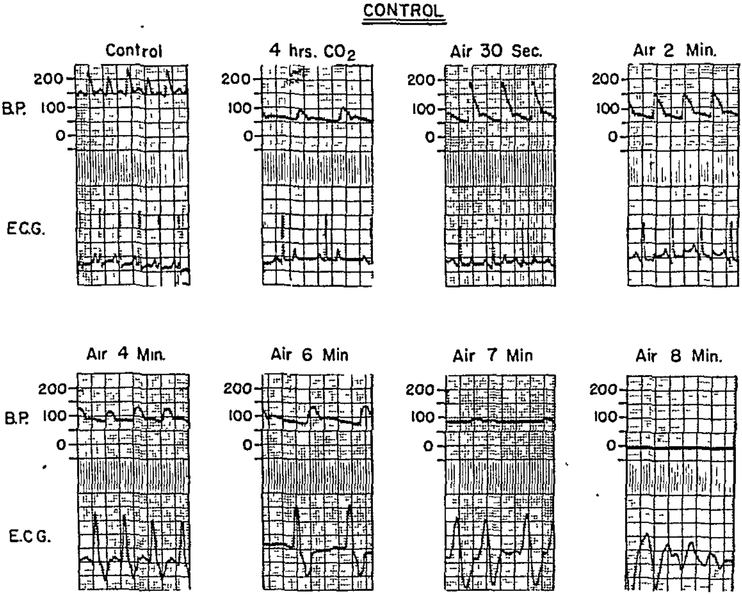

FIG. 1.—Lead II electrocardiographic and blood pressure tracings in a control experiment.

Samples of arterial blood were taken at regular intervals for chemical analysis, and continous electrocardiographic and arterial blood pressure tracings were obtained.

RESULTS

Controls.—A control experiment was performed, in the manner described above, at intervals throughout the series. Of 15 dogs so tested, 14 developed ventricular fibrillation within 10 minutes after being returned to room air inhalation. Fig. 1 illustrates these results.

Thoracic Sympathectomy.—In 10 dogs, bilateral thoracic sympathectomy and cervical ganglionectomy were performed; via bilateral thoracotomy in 9 dogs. In the remaining animal a sternal splitting procedure was employed. The animals were given a recovery period of 2 weeks before subjecting them to the hypercapnia procedure. Only the animal with the sternal split-type incision exhibited fibrillation; none of the others even demonstrated arrhythmias.

A control study for the sympathectomy series was performed by subjecting 5 dogs to bilateral thoractomy without denervation. None fibrillated. Our only explanation for these results is that lateral thoracotomy interferes, probably because of adhesions, with the adequate respiratory exchange necessary for this procedure. The fact that the only dog to fibrillate had had a sternal split-type incision, a procedure resulting in only a minimal disturbance of pulmonary mobility, lends support to this thesis.

An experiment to test the posthypercapneic effect on the same day as the sympathectomy was performed. These animals were intolerant to the carbon dioxide exposure and most of them fibrillated during the hypercapneic period. Table I presents the results of the sympathectomy experiments.

TABLE I. EVALUATION OF SYMPATHECTOMY UPON POSTHYPERCAPNEIC VENTRICULAR FIBRILLATION

	NO. OF EXPERIMENTS	VENTRICULAR FIBRILLATION
Controls	15	14
Thoracic sympathectomy	10	1
Controls, token thoracotomy	5	0
Procedure immediately after sympathectomy; chest not closed	9	7 (Fibrillation occurred while on CO_2)

The ventricular fibrillation threshold, as measured by Shumway and his co-workers[4] employing an electrical stimulus, was measured in 2 dogs both

TABLE II. FIBRILLATION THRESHOLD BEFORE AND AFTER SYMPATHECTOMY

		DELAY (MSEC.)	MILLIAMP.	pH	TEMP.	BLOOD PRESSURE (MM. Hg)
No. 1						
Control		100	15	7.61	37.5	115/80
Left sympathectomy	(1)	110	13	7.46	37.5	100/75
	(2)	95	15	7.36	37.3	150/80
Right sympathectomy	(1)	100	15	7.5	37.5	115/75
	(2)	95	13			
No. 2						
Control		90	20	7.66	36.5	105/75
Right sympathectomy		95	24	7.57	36.0	80/55
Left sympathectomy		110	20	7.62	36.0	85/60

before and after cardiac sympathectomy.* No alteration in the fibrillation threshold was observed as will be noted in Table II.

Sympathetic Blocking Agents.—Dibenzyline in doses of 2 mg./Kg. was injected intravenously in 7 dogs 15 hours before subjecting them to carbon dioxide inhalation to test the effect of inactivation of the sympathoadrenal system on the development of ventricular fibrillation. Five of these animals fibrillated and the remaining 2 [illegible] marked arrhythmia.

Infusion of Calcium Ions.—Calcium gluconate was administered intravenously to 12 dogs: 2 Gm. were given during the period of hypercapnia and 1 Gm. during the ventilation with air. No dog thus treated fibrillated, and

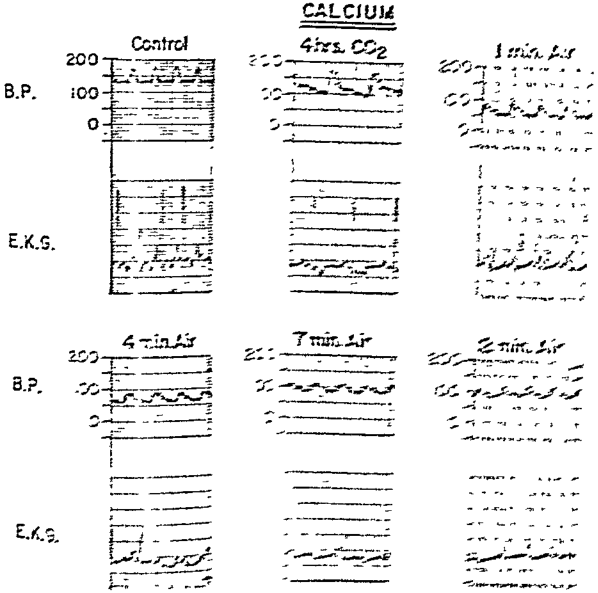

Fig. 2.—[illegible] intravenous [illegible] minimal [illegible] of the calcium [illegible]

arrhythmias [illegible] pressed by [illegible] by Fig. 2.

Infusion of Magnesium [illegible] sulfate in [illegible] though in 3 of [illegible] strated in Fig. 2. [illegible]

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*We are [illegible]

Suppression of Serum Potassium Levels.—The work of other investigators has suggested that suppression of the serum potassium rise during the posthypercapneic state would lessen the incidence of fibrillation.[5, 6]

Because severe respiratory acidosis is associated with hyperglycemia (Table III), we decided to use insulin to suppress this blood sugar rise. Dosage was difficult to estimate and, if excessive, resulted in an extreme drop in blood glucose levels and an inability to tolerate the carbon dioxide inhalation per se. An approximate measure of blood glucose levels was obtained rapidly by the use of blood sugar test paper.

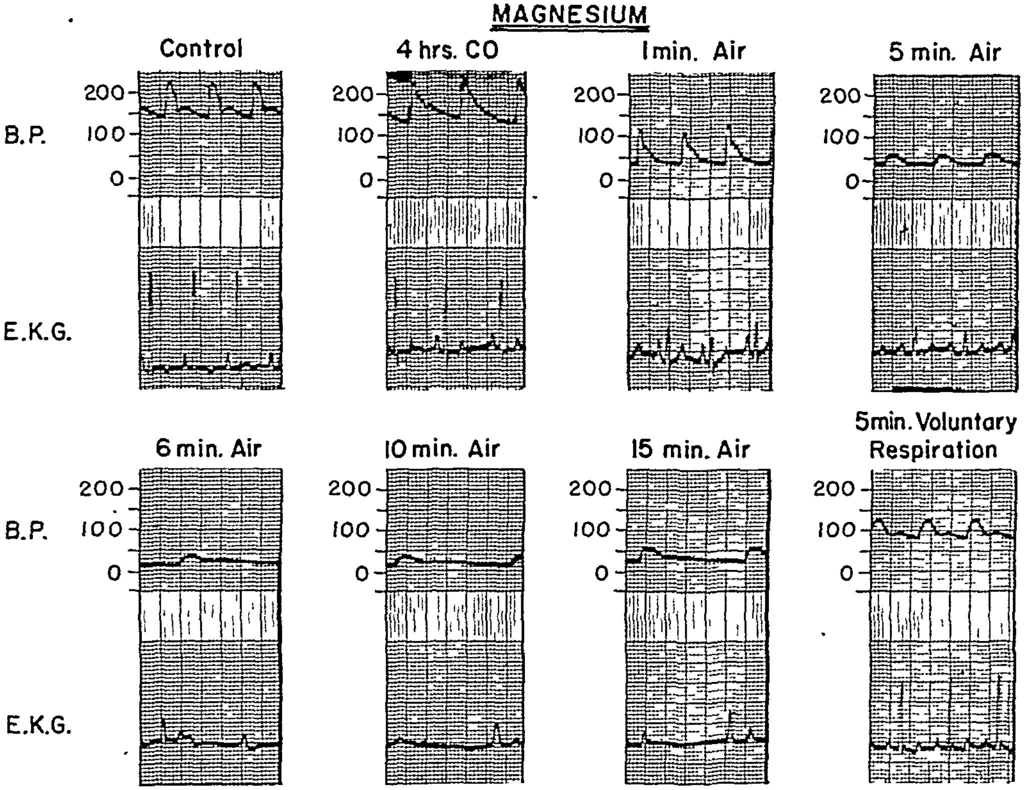

Fig. 3.—Lead II electrocardiograph and blood pressure recording of posthypercapneic dog treated with intravenous infusion of magnesium sulfate. These dogs did develop arrhythmias and other electrocardiographic changes and marked blood pressure depression as illustrated by this tracing, but none of the animals fibrillated.

TABLE III. AVERAGE CHANGES IN LEVELS OF SERUM, POTASSIUM, PHOSPHORUS, AND SUGAR DURING HYPERCAPNIA

	POTASSIUM (MEQ./L.)		PHOSPHORUS (MG. %)		SUGAR (MG. %)	
	CONTROL	4 HR.	CONTROL	4 HR.	CONTROL	4 HR.
Control						
15 dogs	5.2	8.3	4.5	13.9	79	249
Standard deviation	(1)	(2.4)	(1.4)	(2.4)	(11)	(94—Range 134-425)
Dibenzyline						
7 dogs	3.8	7.5	4.6	13.0	76.8	249
Standard deviation	(.06)	(.09)	(1.1)	(3.1)	(148)	(84—Range 176-425)
Corticoid Preparations						
12 dogs	4.5	7.8	4.8	14.3	68.8	250
Standard deviation	(1.9)	(3)	(1.2)	(4.3)	(17)	(42—Range 205-355)

Eight dogs given regular insulin in dosage sufficient to maintain the blood glucose at near control levels tolerated the entire procedure and did not fibrillate. Fig. 4 is typical of the results in the insulin series The effects on the blood levels of glucose, phosphorus, and potassium can be seen in Table IV. It is evident that the use of insulin prevents the gross elevation of the serum potassium level, but does not reduce the rise in phosphate

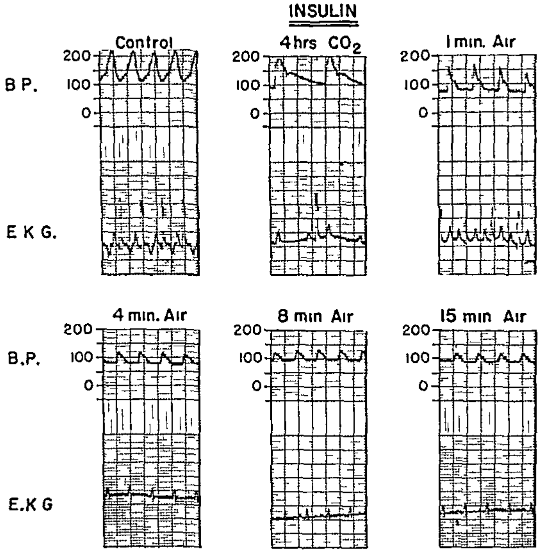

Fig 4—Typical Lead II electrocardiographic and blood pressure pattern of a dog treated with insulin during acidosis Arrhythmias were minimal in all such experiments and blood pressure did not show the typical severe depression

TABLE IV. EFFECT OF INSULIN UPON THE BLOOD CHEMISTRY DURING HYPERCAPNIA

EXPER NO	INSULIN DOSE (UNITS)	POTASSIUM (MEQ /L) CON-TROL	4 HR	PHOSPHORUS (MG. %) CON TROL	4 HR.	GLUCOSE (MG %) CON TROL	4 HR	pH	RESULTS*
1	10	5.1	6 6					6 69	did not fibrillate
2	10	3 5	4 5	3 3	7 5	85	365	6 73	did not fibrillate
3	20					90	148	6 7	did not fibrillate
4	20	4 5	5 7	5 3	24	100	143	6 65	did not fibrillate
5	25	4 6	4 8	3 2	24	82	30	6 77	did not fibrillate
6	20	3 8	5 4	4 5	24	71	260	—	did not fibrillate
7	30	5 1	4 6	3 3	14 5	82	125	6 76	did not fibrillate
8	40	3 8	3 0	4 6	14 5	71	16	6 67	did not fibrillate
Averages		4 3	4 9	4 0	18 1	83	155 3		

*Arterial blood pH obtained just before switch to room air

Corticoid Preparations.—These drugs are known to lower the levels of serum potassium and inorganic phosphate in normal animals. They were, therefore, used in an attempt to suppress the levels of these substances during hypercapnia. Two dogs were given an intravenous dose of alphafluorhydrocortone, 1 mg./Kg., 2 hours before the procedure. Fibrillation was not prevented.

Hydrocortone was given intravenously to 10 dogs 2 to 4 hours before the procedure. Dosage varied from 50 to 200 mg. Six of the dogs fibrillated. The results as seen in Table III show that Hydrocortone, in the dosage used, is not significantly beneficial and did not prevent the rise in the levels of serum, potassium, and inorganic phosphorus. It is possible that the effect of these drugs in this regard is inhibited by acidosis.

Quinidine.—Holland[7] has suggested that the antiarrhythmic action of quinidine might be due to depression of the outward flux of potassium across the myocardial cell membrane. Quinidine gluconate, 10 mg./Kg., was administered intravenously to 2 dogs 20 minutes before reversal of the hypercapnia and both fibrillated. Of 6 dogs given quinidine gluconate, 20 mg./Kg., 30 minutes before reversal, 4 fibrillated.

The results of all of these experiments with the changes in blood chemistry are summarized in Tables III, IV, and V.

TABLE V. THE INCIDENCE OF POSTHYPERCAPNEIC VENTRICULAR FIBRILLATION FOLLOWING VARIOUS EXPERIMENTAL PROCEDURES

PROCEDURE	NO. OF EXPERIMENTS	VENTRICULAR FIBRILLATION
Controls	15	14
Calcium gluconate	12	0
Insulin	8	0
Cortisone	12	8
Dibenzyline	7	5
Quinidine	8	6
Magnesium	6	0

DISCUSSION

The maintenance of normal transmembrane potentials in resting cells requires a very definite partition of ions. Calcium and potassium imbalance in particular greatly affect the permeability and excitability of all cardiac tissue and the relative concentration of these ions are as important as the absolute.[8] Whatever the precipitating factors may be, it would seem that sudden changes in ion flux are of extreme importance in the genesis of ventricular fibrillation. Brown and Prasad[2] have shown that in the posthypercapneic dog the ratio of ionized calcium and potassium drops rapidly to nearly one third of normal. Blood samples from the coronary sinus of dogs subjected to hypothermia were found by Covino to show a decrease in ionized calcium and an increase in potassium immediately prior to fibrillation. These changes were not present if the dog did not fibrillate.[9] According to Cherbakoff, when the descending branch of the left coronary artery is ligated to produce fibrillation, there is a marked rise in the level of potassium in the coronary sinus preceding the onset of fibrillation. However, if the rise in the potassium level is prevented by the administration of insulin and glucose, or bicarbonate, fibrillation is prevented in a high proportion of the animals tested.[10]

The success of calcium, magnesium, and insulin in blocking fibrillation would appear to confirm the importance of an altered myocardial ionic balance in the etiology of fibrillation. Not only did the administration of calcium prevent fibrillation, but severe arrhythmias did not occur. The beneficial effects of magnesium support the contention that this ion has some similarity of action to calcium upon the myocardial cells, especially when the calcium levels are below normal.[8]

The participation of the sympathetic nervous system in response to carbon dioxide stimulation has been adequately demonstrated by Tenney[3] and Fenn.[11] The fact that the metabolic changes of hyperkalemia, hyperphospheremia, and hyperglycemia that occur during the hypercapnia, can also be obtained by Adrenalin administration suggested the use of Dibenzyline to suppress any hyperactivity of the sympatho-adrenal system during carbon dioxide inhalation. However, this sympatholytic agent prevented neither the fibrillation nor the metabolic alterations. Caution must be employed in the interpretation of such results since complete obliteration of this system might not have been obtained by the pharmacologic methods employed.

We believe that the results of our denervation experiments would not substantiate the use of sympathectomy for the prevention of fibrillation. This belief was supported by the failure of sympathectomy to prevent fibrillation as produced by the ligation of the circumflex coronary artery in dogs so tested.

As to the role of the cardiac nerves in the development of ventricular fibrillation, it should be noted that cervical vagotomy had no protective influence on the development of ventricular fibrillation by the experimental method herein employed.

SUMMARY

1. The administration of calcium ions successfully prevented posthypercapneic fibrillation.

2. The administration of magnesium sulfate similarly prevented posthypercapneic fibrillation in all animals so tested.

3. Insulin was successful in preventing fibrillation in all of 8 dogs treated. Administration of insulin suppressed the serum levels of both potassium and glucose during hypercapnia, but did not prevent the rise of the phosphate ion.

4. Corticoid preparations did not suppress the levels of serum potassium and inorganic phosphorus during hypercapnia. Of 12 dogs treated only 4 failed to fibrillate.

5. Quinidine, administered to 8 dogs, failed to prevent fibrillation in 5 of these.

The authors wish to gratefully acknowledge the technical assistance of Mr. [illegible] [illegible]ther and Earl Levens in performing these experiments.

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DISCUSSION

(PAPERS BY MAGOVERN [PAGE 561], SMITH [PAGE 573], KANTROWITZ [PAGE 586], BRECKLER [PAGE 594], STEPHENSON [PAGE 604], NELSON [PAGE 610], GORDON [PAGE 618], GOOTT [PAGE 630], AND THEIR ASSOCIATES)

DR. HENRY SWAN, II, Denver, Colo.—I would like to make a comment or two regarding the very interesting papers on ventricular fibrillation, which I thought were all extremely productive this morning, and I want to compliment the authors on them.

In regard to the relationship of the central nervous system to fibrillation, I think we should remind ourselves of some interesting work which has gone on in the past, and to ask ourselves how to relate this information to some of the interesting work we heard this morning. I thought Dr. Nelson particularly might like to comment on this.

A year and a half ago, Dr. Montgomery and I, at the Pump-Oxygenator Conference in Chicago, discussed the pharmacology of the heart, and emphasized that the sympathetic innervation to the heart appeared to play an important role in the ability of the heart to undergo ventricular fibrillation when induced by various means.

In 1930, and for a period of several years, Meakin and his co-workers at Wisconsin were studying this problem and the interesting relationship of the actual chemical formula to some of the sympathomedic agents was worked out.

This slide simply shows that the dihydroxy catechol amines, of which adrenalin is a typical example, are fibrillogenic agents, whereas the monohydroxy catechol amines, such as neosynephrine, are not. Thus, there is a definite relationship between the chemical formula and its reaction on the heart.

These workers studied sympathectomy in relation to the stimulus from these dihydroxy catechol amines and they found that if you take out the sympathetic chain down to T-7 you have protected the heart to a large extent from fibrillation induced by catechol amines. But the same effect was also achieved if you left the sympathetic system intact but decerebrated the animal slightly above the midbrain.

Thus, it would appear that the integrity of the sympathetic nervous system to above the level of the midbrain is probably important in the regulation of the ability of that heart to fibrillate.

It is interesting to me that the heart in Dr Nelson's case was isolated and in this respect I would like to ask him if he feels that this is of any importance in his experiment On the other hand, Dr Goott and his co workers all showed this morning that another stimulus is affected by this sympathetic denervation, namely that of the rapidly changing potassium ion induced by rebreathing after CO

DR AKE SENNING, Stockholm, Sweden—First, I wish to take this opportunity to thank you for letting me attend this meeting as a guest It has really been a fascinating meeting

Second, I wish to convey warmest regards from my teacher and chief, Clarence Crafoord, especially to the older members of this Association I do understand his enormous admiration for American thoracic surgery, having visited many of your clinics

Today I should like to discuss the paper of Stephenson, Edwards, Jolly, and Scott We have been working with different types of pacemakers outside the patient and inside the patient to treat complete A V blocks, but we have not been especially happy with any *of these types of pacemakers*

The last gadget we have is the one I have in my hand here, as big as a watch, and we have used this experimentally in animals and clinically in 1 case, placing it subcutaneously in the epigastrium This transistor pacemaker is charged at intervals from the outside by a cord that we place around the patient, and if we wish we can trigger the pacemaker to any desired rhythm with a special induction coil outside

But we are not pleased with this either, because we have had the same experience as all other people have, that after a while the resistance in the heart, or whatever it is, increases more and more, so that a higher and higher voltage is required, and when one reaches the neighborhood of 20 volts the whole patient jumps, but the heart goes its own rhythm This takes about 4, 5, or 6 weeks So I don't think this is the way to tackle this problem I think we have to seek other ways to treat an A V block for long periods

DR JOHN R DERRICK, Galveston, Texas—I would like to discuss the paper of Dr Nelson in regard to the tranquilizers and their use in preventing cardiac arrythmias

We have had some experience with a tranquilizer by the name of mepazine, one of the phenothiazines We used it originally in a group of experiments to prevent fibrillation in cooling animals to cardiac standstill

[Slide] We premedicated the animals with mepazine, and found that in 45 per cent we could take them down to standstill and successfully resuscitate the animals One of the disquieting things, however, was that in several instances it required tremendous doses of Adrenalin to resuscitate these animals In two instances we used as much as 30 and 40 c c of 1 1000 Adrenalin

This demonstrates the cooling process, and you can see the progressive drop in the blood pressures and a progressive slowing of the electrocardiogram down to the point of standstill

[Slide] In resuscitating the animal, there is a progressive increase in the pulse rate with rewarming and intravenous Adrenalin We frequently observed a profound hypotension following resuscitation

We cooled 43 animals by this technique and were able to resuscitate 45 per cent We have used mepazine clinically in 16 instances, and have found that, in each instance, if it was given as a premedication, the patient seemed to do rather well We have used it in 5 instances at the time of surgery, and in all 5 the patients developed profound hypotension The tranquility of the patient was very alarming in these instances

I would like to compliment Dr Nelson on his excellent work using a very difficult experimental technique

DR DERMONT W MELICK, Phoenix, Ariz—My remarks are directed toward the cardiac stimulator, Paper No 19 I am not quite as pessimistic as our Scandinavian friend

This is a report of a 50-year-old man with cardiac asystole lasting as long as 30 seconds, complete heart block, and treatment consisted of insertion of a silver wire into the right ventricle and an indifferent electrode in the left axilla. This miniature cardiac pacemaker was obtained through the good offices of Dr. Ehrlich and Dr. Lillehei. This man was on the stimulator for 4 months. At times it was thought it should be stopped, but the patient would not allow it to be stopped. He played golf (without permission); the stimulator stopped by itself at the end of 4 months. At the present time, his rate is 60. He does not have any more periods of syncope.

The only trouble we have had is with the electricians' union, who say we should have a union card for this sort of wiring.

DR. ROBERT S. CARTWRIGHT, Albuquerque, N. M.—We certainly agree with others that tissue hpoxia is the demonstrated principal cause of metabolic acidosis in extracorporeal circulation, and that high flow, normocapnial perfusions using non-acidotic donor blood will usually eliminate metabolic acidosis as a problem. However, we feel it is worth emphasizing that there are other sources of acidosis. Among these is glycolysis, which occurs in extracorporeal blood either before or after perfusion; lacticacidemia which may result from respiratory alkalosis either before or during perfusion; and the possibility of an inadvertent low flow due to arterial cannula obstruction, caval cannula occlusion, or mechanical failure. Acidosis also can occur due to metabolic disease, or renal disease, and is known to exist in patients having cyanotic heart disease. It is common to most major surgical procedures.

Consequently, we feel acidosis should be considered a factor in extracorporeal circulation. Systems in which pH, for example, is used to control the per cent of carbon dioxide in the oxygenator gas mixture will inevitably lead to a hypocapnial perfusion when metabolic acidosis does develop.

Another factor which became evident in our studies was that the use of the Clark electrode in monitoring the venous saturation can lead to inaccurate conclusions since it deals with the vertical portion of the hemoglobin dissociation curve, where pH, pCO_2, and temperature have a marked influence on the relationship between pO_2 and hemoglobin saturation.

DR. HARRISON BLACK, Boston, Mass.—I would also like to discuss the matter of metabolic acidosis occurring during extracorporeal circulation. On the basis of recent experience at Brigham Hospital in Boston, Dr. George Albertal, who has been working with us, introduced a useful change in perfusion technique in an attempt to reduce the degree of this acidosis. Originally we have used 3 per cent CO_2 and 97 per cent O_2 in our Kay-Cross oxygenator. With this mixture normal pCO_2 values in the blood were maintained. However, the pH values fell, the flow was only barely adequate, and the peripheral resistance was elevated. At the end of such perfusions we found an average pH of 7.26 and a bicarbonate level of 17. Two hours later these values had improved only slightly.

In the last 20 cases we have used 100 per cent O_2 in the oxygenator in the hope of compensating for the metabolic acidosis. We have been gratified to find that, while the arterial pCO_2 has droppèd into the low 30's, the pH at the end of the run has averaged 7.45. Although the bicarbonate values have still been low (average 16), indicating that there is still some acidosis, the resistance figures have dropped to normal and the patient appears to be able to correct the deficit postoperatively. Thus, 2 hours after the conclusion of such a perfusion the pH has averaged 7.39 and the bicarbonate has risen to 23. The pump flows in these patients have similarly increased from 84 per cent of the preoperative cardiac output when 3 per cent CO_2 was used to 102 per cent with pure oxygen. The suggested beneficial effect on pump flow is being further studied.

DR. J. ANKENEY, Cleveland, Ohio.—I would like to discuss Paper No. 14 and congratulate Dr. Magovern and his associates on a very nice piece of work.

My remarks are very similar to those of Dr. Black. We observed in the laboratory that using 100 per cent oxygen in our Kay-Cross oxygenator, carbon dioxide washout does not occur, and pH remains more or less constant. Therefore, we elected to omit carbon dioxide in a group of 36 patients and compare the results in this group with 22 patients in which 2 per cent carbon dioxide and 98 per cent oxygen was used.

[Slide] We found that in those cases in which oxygen alone was used, the pCO_2 and pH remained relatively stable throughout the period of perfusion This was true even if total bypass was carried out over 50 minutes On the other hand, when 2 per cent carbon dioxide was added to the oxygenator, the pH fell and the pCO_2 rose. We, therefore, concluded that it was not necessary to add carbon dioxide to the oxygenator during total bypass. When carbon dioxide was added, a respiratory acidosis was imposed upon metabolic acidosis which develops to some degree during perfusion

DR. CONSTANTIN G. CHARONIS, Baltimore, Md —I want to congratulate Dr Kantrowitz for his inexpensive pump oxygenator. I am taking the opportunity to tell you just a few words about the oxygenator that we have developed at the University of Maryland in Baltimore

Our oxygenator is a disposable disc oxygenator. It has all the advantages of the standard disc oxygenator. It is made of plastic material and comes in packages like intravenous sets, ready to be used. Specialized technicians are not necessary for cleaning and care of the oxygenator We exhibited our oxygenator last year in Boston, and 2 weeks ago we presented complete data about the oxygenator at the meeting of the Society for Artificial Internal Organs, and will appear in Volume 5 of their transactions.

The entire system, including the disc oxygenator, the tubing, and the bubble filter, costs a little more than $30 plus the cost of sterilization and the shipping

DR THOMAS F. NEALON, JR, Philadelphia, Pa —I would like to say a few words about the very nice presentation of Dr. Smith and his co workers on the problem of a blood preservative

He pointed out the need for a better method of preserving blood and also the desirability of a method of converting blood stored in ACD solution to the equivalent of freshly heparinized blood. He also indicated difficulties associated with this

We have attempted to approach this in a somewhat different manner. [Slide] This has been accomplished by passing the blood over ion exchange resin columns This slide represents the chemical values in dog's blood before and after storage Immediately after it was collected and combined with ACD solution, there was a marked drop in the pH, an increase in sodium, and a considerable addition of citrate

After this blood was stored for 21 days the most important change was the accumulation of potassium and of ammonium. However, in the meantime, because of the increase in lactic and pyruvic acid, as well as phosphates, the pH had dropped further to 6 02. This blood was then passed over two ion exchange resin columns, a cation, and an anion column Following this, practically all the potassium and citrate were removed, as well as half of the ammonium, phosphate, and lactate As a result of this, the pH was then brought from 6 02 to 7 0

This represents just a preliminary study on this work We have used this blood for exchange transfusions to date in 3 animals They have tolerated it without any hemorrhagic effects, and within 24 hours all of these chemical studies were normal

DR WILFORD B NEPTUNE, Boston, Mass —With regard to the problem of donor blood, I would like to mention a technique which we are using with a bubble type oxygenator which at least has proved successful in our hands We are no longer using any donor blood whatsoever for priming the pump oxygenator system nor for support during the perfusion itself The only blood which the patient receives is ordinary citrated bank blood to replace blood loss from the operative procedure and postoperatively for pleural drainage

[Slide] This is a selected group of patients to demonstrate various age groups and various body weights, going from 6 to 66 and from a weight of 55 pounds to 159 pounds

These patients have all been perfused at rates of 65 to 80 c.c. per kilogram per minute. We have done various types of monitoring and physiologic studies and, at least to our interpretation, can demonstrate no adverse disadvantages with this technique.

You can see the types of lesions repaired, and the perfusion times have varied from 15 minutes to a little over 1 hour. In our experience, in perfusions under 30 minutes, we usually use about one or two pints of blood during the procedure and one pint in the next 24 hours to cover pleural drainage. In perfusions from 30 minutes up to an hour or an hour and a half we use three to four pints of blood during surgery and usually one postoperatively.

I call your attention to the 1 patient who received three pints of blood postoperatively. In our total experience, this patient has received the largest single volume of blood during an open heart procedure. The average patient having open heart work on our service receives a total volume of blood which is less than the average patient having a pulmonary resection and, moreover, it is ordinary citrated bank blood and, at least in our experience, we have minimized the problem of procurement, storage, and waste.

DR. THOMAS J. E. O'NEILL, Philadelphia, Pa.—In Paper No. 18, it was stated that there were three principles involved in the currently available heart pumps. I should like to present a fourth type.

This particular principle and invention goes back many centuries ago and was developed first by Archimedes.

[Slide] It differs from the other three principles as the jet airplane engine differs from the old-time piston engine. I am surprised that the aircraft industry didn't think of it first.

Among its advantages is the small size. The largest diameter is less than 8 inches. Its priming volume necessarily is very small. It is quiet in operation and vibrationless. Its output can be regulated carefully from 300 c.c. per minute to 14,000 c.c. per minute.

[Slide] It is easy to clean. It is completely autoclavable, made up of mostly stainless steel and a plastic inner liner, and it can be assembled and dissembled without any tools, just using the fingers, putting together the end plates on slots.

The turbine is a modification of the old water pump of Archimedes, and you can see it here. It rides in the inner lining, which is housed in the outer cylinder. There is a space between these two in which you can circulate fluids to regulate temperatures at any desired level.

Its principal operation: The blood will flow in this direction; rotating on its long axis it effects propulsion, without any valves, by a pulling action, a pushing action, and some centrifugal force. We feel that this is definitely superior to any of the ones presented so far.

A METHOD FOR THE SIMULTANEOUS MEASUREMENT OF MAXIMUM BREATHING CAPACITY, PULMONARY VOLUMINA, AND EFFECTIVE LUNG VENTILATION

George W. Wright, M.D., and Saul R. Gilford (by invitation),*
Cleveland, Ohio

IN THE PRACTICE of medicine, information concerning the effectiveness with which the lungs can be ventilated under varying stresses is frequently desired. Measurement of volitional maximal rate of air flow, of distribution of inspired gas, and of the degree to which the lungs can be filled and emptied, will disclose, quantitate, and localize impairments of ventilation, but the time consuming nature of these measurements has discouraged their widespread application. To minimize this barrier, we have designed and assembled an apparatus to measure simultaneously the maximum breathing capacity (MBC), pulmonary volumina, and a factor reflecting alveolar ventilation. To prepare the apparatus, carry out the test, and make the calculations requires approximately 5 minutes for a single determination.

METHOD

A spirometer inside of which is placed a bag containing 6 L. of oxygen, a meter for continuous analysis of nitrogen, and suitable recording equipment comprises the apparatus. The subject exhales maximally and is then connected to the bag, containing 6 L. of pure oxygen, inside the spirometer. A single full inspiration from the bag records the vital capacity. The MBC is now measured over a 15 second period by rebreathing to and fro in the bag. During this procedure the bag and lung gases come to, or approach, nitrogen equilibrium. At the end of the maximum breathing capacity a maximal exhalation is made into the bag and the subject is turned out of the spirometer. The nitrogen concentration at the mouth is constantly sampled and analyzed and at the termination of the procedure, the nitrogen concentration in the bag is measured by expelling the bag's contents past the sampling point. From these data the residual volume is calculated in the conventional manner for the closed circuit method.[1] No correction for nitrogen excretion or oxygen absorption was made. Knowing the residual volume and the number and volume of

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From the Department of Medical Research St. Luke's Hospital Cleveland Ohio.

Read at the Thirty-ninth Annual Meeting of The American Association for Thoracic Surgery at Los Angeles Calif. April 21-23 1959.

*Consultant in Instrumentations and Electronics.

These patients have all been perfused at rates of 65 to 80 c.c. per kilogram per minute. We have done various types of monitoring and physiologic studies and, at least to our interpretation, can demonstrate no adverse disadvantages with this technique.

You can see the types of lesions repaired, and the perfusion times have varied from 15 minutes to a little over 1 hour. In our experience, in perfusions under 30 minutes, we usually use about one or two pints of blood during the procedure and one pint in the next 24 hours to cover pleural drainage. In perfusions from 30 minutes up to an hour or an hour and a half we use three to four pints of blood during surgery and usually one postoperatively.

I call your attention to the 1 patient who received three pints of blood postoperatively. In our total experience, this patient has received the largest single volume of blood during an open heart procedure. The average patient having open heart work on our service receives a total volume of blood which is less than the average patient having a pulmonary resection and, moreover, it is ordinary citrated bank blood and, at least in our experience, we have minimized the problem of procurement, storage, and waste.

DR. THOMAS J. E. O'NEILL, Philadelphia, Pa.—In Paper No. 18, it was stated that there were three principles involved in the currently available heart pumps. I should like to present a fourth type.

This particular principle and invention goes back many centuries ago and was developed first by Archimedes.

[Slide] It differs from the other three principles as the jet airplane engine differs from the old-time piston engine. I am surprised that the aircraft industry didn't think of it first.

Among its advantages is the small size. The largest diameter is less than 8 inches. Its priming volume necessarily is very small. It is quiet in operation and vibrationless. Its output can be regulated carefully from 300 c.c. per minute to 14,000 c.c. per minute.

[Slide] It is easy to clean. It is completely autoclavable, made up of mostly stainless steel and a plastic inner liner, and it can be assembled and dissembled without any tools, just using the fingers, putting together the end plates on slots.

The turbine is a modification of the old water pump of Archimedes, and you can see it here. It rides in the inner lining, which is housed in the outer cylinder. There is a space between these two in which you can circulate fluids to regulate temperatures at any desired level.

Its principal operation: The blood will flow in this direction; rotating on its long axis it effects propulsion, without any valves, by a pulling action, a pushing action, and some centrifugal force. We feel that this is definitely superior to any of the ones presented so far.

A METHOD FOR THE SIMULTANEOUS MEASUREMENT OF MAXIMUM BREATHING CAPACITY, PULMONARY VOLUMINA, AND EFFECTIVE LUNG VENTILATION

George W. Wright, M.D., and Saul R. Gilford (by invitation)*
Cleveland, Ohio

In the practice of medicine, information concerning the effectiveness with which the lungs can be ventilated under varying stresses is frequently desired. Measurement of volitional maximal rate of air flow, of distribution of inspired gas, and of the degree to which the lungs can be filled and emptied will disclose, quantitate, and localize impairments of ventilation, but the time-consuming nature of these measurements has discouraged their widespread application. To minimize this barrier, we have designed and assembled an apparatus to measure simultaneously the maximum breathing capacity (MBC), pulmonary volumina, and a factor reflecting alveolar ventilation. To prepare the apparatus, carry out the test, and make the calculations requires approximately 5 minutes for a single determination.

METHOD

A spirometer inside of which is placed a bag containing 6 L. of oxygen, a meter for continuous analysis of nitrogen, and suitable recording equipment comprises the apparatus. The subject exhales maximally and is then connected to the bag, containing 6 L. of pure oxygen, inside the spirometer. A single full inspiration from the bag records the vital capacity. The MBC is now measured over a 15 second period by rebreathing to and fro in the bag. During this procedure the bag and lung gases come to, or approach, nitrogen equilibrium. At the end of the maximum breathing capacity a maximal exhalation is made into the bag and the subject is turned out of the spirometer. The nitrogen concentration at the mouth is constantly sampled and analyzed and at the termination of the procedure, the nitrogen concentration in the bag is measured by expelling the bag's contents past the sampling point. From these data the residual volume is calculated in the conventional manner for the closed circuit method.[1] No correction for nitrogen excretion or oxygen absorption was made. Knowing the residual volume and the number and volume of

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each breath, a factor reflecting ventilation effectiveness can be calculated. The tidal volume during nitrogen equilibration can be measured directly or estimated by dividing the total volume respired by the number of breaths taken during the equilibration period.

For purposes of comparison, the MBC was also measured in the conventional manner by volitional maximal hyperventilation for 15 seconds through a face mask and Rudolph (high velocity) valve into a Douglas bag connected by flexible tubing 60 cm. long and 4 cm. in diameter. The conventional open circuit, nitrogen washout method[2] was used for measuring the functional residual capacity and a 13.5 L. Collins spirometer for spirometry. Nitrogen concentration was determined by the Van Slyke apparatus.

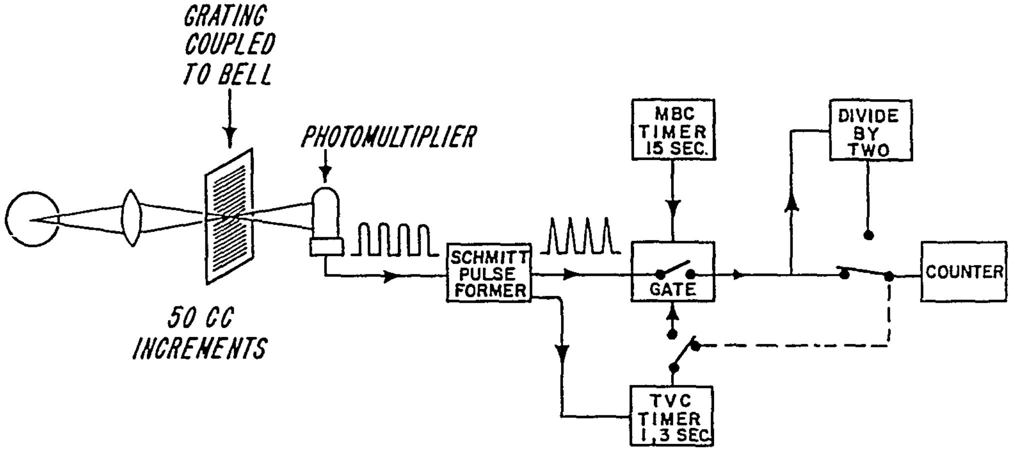


Fig. 1.—Computer channel. Line drawing of signal generator. The light source and grid are contained inside the Krogh type spirometer.

APPARATUS

The spirometer is of the Krogh type, having a bell top measuring 38 x 50 cm., and not counterbalanced. To avoid the inaccuracies imposed by the load and inertial effects of contact writing systems, and to provide a means for immediate display of single (vital capacity) or the sum of multiple (MBC) bell excursions, an optical system was designed for the conversion of bell motion to a measurable signal. In Fig. 1 a block diagram of the instrument is shown.

A light source projects a small spot against a mask having a series of opaque and transparent lines. Each space between the lines represents a volume increment of 50 c.c. and the movement of the mask produces one light pulse for each 50 c.c. deflection. The light pulses are received and amplified by a photomultiplier tube and fed to a Schmitt trigger circuit which generates a sharp electrical pulse for each light pulse. These are fed to the counter circuit through a "gate" system. The "gate" is controlled by a timer circuit permitting pulses to be counted only during the timing interval. For the MBC measurement, a 15-second time interval is used. For timed vital capacity measurements, a 1 or 3 second interval is selected through a special timer which starts its timing interval only after the first pulse is received At the same time the counts are passed through a 'divide by two circuit" to make the displayed results direct indicating The counts are fed into a simple computer in the form of a digital counter for adding up the volume increments with proper provision for multiplication of appropriate factors The results are displayed directly on a counter dial which reads in liters per minute for the MBC measurement, and in fractions of liters for the vital capacity measurements A second and independent system and circuitry produces an output directly proportional to volume as in a conventional spirometer This consists of an optical system similar to that of the digital channel but with a mask that is a linearly tapered slot The amount of light reaching the photocell is a function of the position of the mask and is directly related to the deflection of the bell and therefore to the volume This channel is used where spirometer patterns are of interest such as recording the tidal volume and changes in mid-position The output of this channel must be fed into some form of recorder such as an oscilloscope The spirometer and its signal producing and recording system will be described in technical detail in a subsequent publication

Continuous sampling of gas was done at the spirometer end of the tubing connecting the face mask with the bag inside the spirometer The continuous sample was passed through a Water's nitrogen analyzer and recorded on a Texas direct writer The spirometer channel signaling the tidal volume was also recorded on the Texas direct writer The response time of the nitrogen meter is less than 0 05 second, and the frequency of the Texas writer is 15 per second

CRITIQUE OF SPIROMETER AND ITS RECORDING APPARATUS

In the mid position, the bell of the spirometer exerts a static pressure not exceeding 2 mm of water The response of the spirometer to volume changes initiated by a mechanical pump of the piston type is shown in Fig 2 There is a flat response over a range of 40 to 80 cycles per minute with a stroke of 3 L The peak pressures under the bell during inspiration and expiration at various MBC are shown in Fig 3 It is of interest to compare the pressures under the bell to peak pressures under the face mask at similar MBC as is shown in Fig 4 The mask is attached to the spirometer by a piece of flexible tubing, 18 cm long and 2 5 cm in diameter at the narrowest portions Of further interest is a comparison of the pressures beneath the face mask when attached to the Krogh spirometer to pressures beneath the face mask when the MBC is being measured through a conventional high velocity (Rudolph) valve and Douglas bag combination (Fig 4) It is apparent from such comparison that the work imposed by internal resistance in the Krogh plus face mask combination is appreciably less than that in the high velocity valve plus Douglas bag combination It would appear from these data that the instrument as described will faithfully record single or summed excursions of the spirometer bell through cycle ranges apt to be met in clinical practice with less instrumental impediment to air flow than exists in some other conventional methods for measuring the MBC.

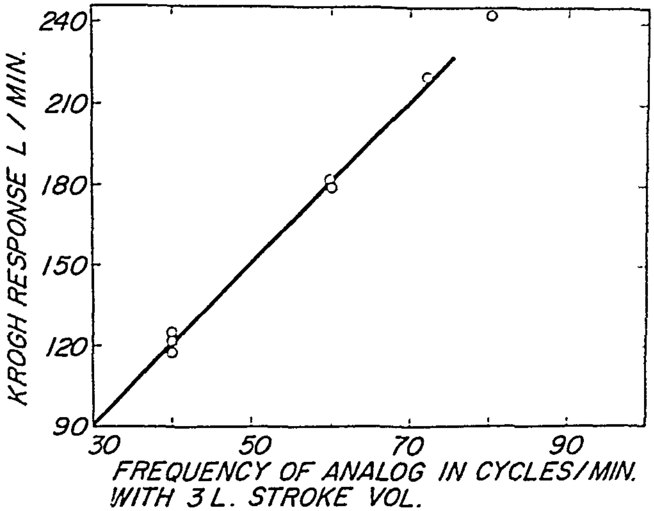
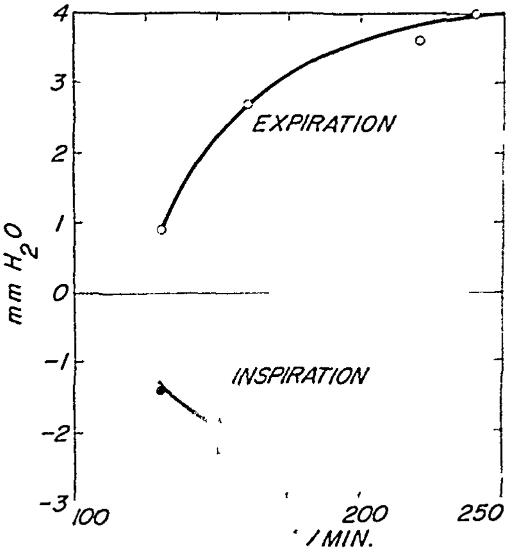


Fig. 2.—Dynamic response of spirometer and counter to mechanically controlled input.



beneat meter bell during various rates of MBC.

ter is such that we do not believe
r stroke volumes faithfully repre-
ough we do not know the precise
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s importance. Ample time for
was provided in making the

terminal expiration and in measuring the concentration of nitrogen in the bag at the end of the run. As a further check, these values were read directly from the nitrogen meter.

COMPARISON OF MBC AND PULMONARY VOLUMINA AS MEASURED BY SIMULTANEOUS AND BY CONVENTIONAL METHODS

A group of normal individuals ranging in age from 17 to 50 years, and a similar group of persons having various degrees of diffuse obstructive pulmonary emphysema, were studied.

As seen in Table I, among normal and abnormal persons, there is a nice agreement between the average MBC as measured conventionally with a high velocity valve and Douglas bag and that measured in the optically recording Krogh spirometer. Both measurements are in close agreement with the mean of the predicted MBC for the normal group. In three instances, the difference as measured by the two methods was greater than 10 L. in normal persons, while in abnormal persons it was never more than 5 L. There was a random scatter of all of the differences suggesting that the apparatus per se did not account for the variation. Some individuals found the Krogh spirometer to be more comfortable whereas others felt the reverse. We anticipated that the shorter connection between the face mask and the immobile spirometer would be a handicap and perhaps it was in some instances. No one complained of resistance in the apparatus used.

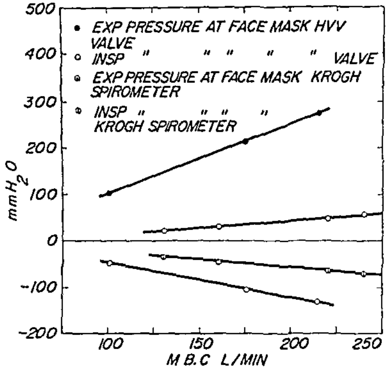

Fig. 4—Peak pressure generated beneath face mask during various rates of MBC initiated by mechanical pump with stroke volume of 3 L as measured by conventional high velocity valve and Douglas bag in contrast to the Krogh spirometer.

The vital capacity of both the normal and the abnormal individuals, as shown in Table I, was essentially the same when measured by the two spirometers. In 4 persons of each group the difference slightly exceeded 250 c.c. but was of a random distribution.

TABLE I. COMPARISON OF MBC AND PULMONARY VOLUMINA AS MEASURED BY THE NEW AND CONVENTIONAL PROCEDURES

	NO.	MEAN BY CONVENTIONAL METHOD	MEAN BY NEW METHOD	DIFFERENCES	MEAN OF DIFFERENCES	MEAN OF PREDICTED VALUES
			Normal Group			
MBC	16	158 L./min.	159	+1	7	152
V. C.	15	4.59 L.	4.52	-0.07	0.26	4.38
R. V.	17	1.13 L.	1.29	+0.16	0.19	1.28
T. C.	15	5.73 L.	5.80	+0.07	0.22	5.59
			Abnormal Group			
MBC	18	46 L./min.	45	-1	4	104
V. C.	11	3.21 L.	3.08	-0.13	0.28	4.04
R. V.	11	3.11 L.	3.01	-0.10	0.51	1.35
T. C.	11	6.31 L.	6.09	-0.22	0.68	5.39

The residual volume is estimated somewhat higher by the rapid method in normal persons as is shown in Table I. The maximum difference in any individual was 300 c.c. In no instance did the rapid method give an estimate significantly larger than the predicted normal figure. This degree of agreement is gratifying because we had anticipated the rapid method to estimate a higher residual volume than that obtained by the conventional method for the following reason. The accuracy of the closed circuit method, in contrast to the open circuit method, is strongly dependent upon the assumption that terminal expired nitrogen concentration truly represents the mean concentration of nitrogen in the lung as a whole at the moment of sampling. Distribution and mixing of inhaled gas is known to be imperfect even in normal persons during slow breathing. During rapid breathing this uneven distribution is augmented, the gas flowing preferentially to areas of lowest airway resistance and largest compliance. Because of this, the terminal expired sample may be obtained from the poorly ventilated area and hence be above the mean nitrogen concentration of the lung. A falsely high terminal expired nitrogen concentration leads to a falsely large residual volume. Of course, it is also possible that the major contribution to the terminal expired nitrogen sample may come from hyperventilated lung tissues. This will lead to a falsely low nitrogen and a falsely small residual volume. The advantage of the open circuit method is that the error caused by poor distribution is minimized because nitrogen is being constantly washed out and, over a 7-minute period, reaches a very low value except in grossly abnormal lungs.

Even in the abnormal group a reasonably good agreement was found between the two methods for measuring residual volume as shown in Table I. As might be anticipated from the above remarks, since uneven distribution and mixing are more severe in emphysematous than in normal persons, the difference between the estimates by the two methods is greater. It will be noted in Table I, that the mean of the differences between the two methods in the residual volumes of the abnormal group is almost three times as great as that of the normals. From a practical point of view, the residual volume cannot be estimated with reasonable accuracy unless equilibrium between the lung and bag is rather closely approximated. A further comment in this regard will be found in the conclusions.

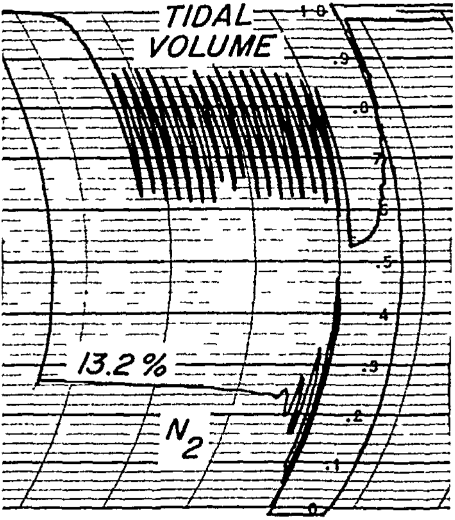

Fig 5—Tracing of tidal volume and of nitrogen concentration in rebreathed gas during MBC measurement in a normal person Read from right to left. Inspiration has down stroke

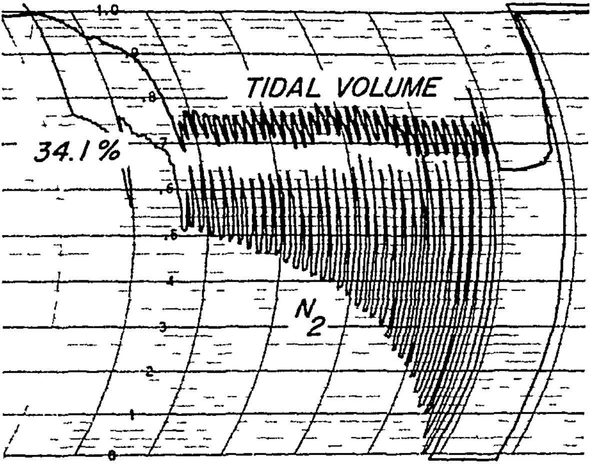

Fig 6—Tracing of tidal volume and of nitrogen concentration in rebreathed gas during MBC measurement in a case of diffuse obstructive emphysema Inspiration has down stroke

No discussion of the estimates of total capacity is needed since this is the sum of vital capacity and residual volume and the above remarks apply.

EFFECTIVE LUNG VENTILATION

In this study two methods were used for estimating effectiveness of lung ventilation. On the basis of inspection alone, it was apparent, as shown in Fig. 5, that the majority of normal persons achieved approximate equilibration in the lung and bag within three to six breaths during the maximum breathing capacity. No normal person required more than seven breaths to effect a nonfluctuating nitrogen concentration. A slight fluctuation undoubtedly occurred but could not be recognized with our equipment. In contrast, as shown in Fig. 6, each person of the abnormal group either failed to come to equilibrium or required more than ten breaths to do so. On the basis of inspection alone, one can separate a normal from an abnormal group. A second method involves the calculation of the theoretical number of breaths required to reach equilibrium based on the residual and tidal volumes. The normal individuals all actually reached equilibrium within one breath of the theoretical number while all of the abnormals required more than the theoretical number of breaths or failed to equilibrate at all. This portion of our study is still under investigation and will form the basis of a subsequent report.

CONCLUSIONS

Our original purpose in devising this equipment and applying the methods was to develop a procedure for the rapid screening of large populations in order to recognize those persons having normal ventilatory powers. Our data indicate that this unit will faithfully record the maximum breathing capacity and vital capacity in normal and abnormal persons. The rapid closed circuit method of measuring residual volume is subject to some error, but is acceptable as a screening procedure for separating normal from abnormal persons. We suggest that in those persons who do not attain nitrogen equilibrium during the maximum breathing capacity, better accuracy could be obtained by permitting them to continue to rebreathe at a lower rate after the maximum breathing capacity has been performed. The test could be prolonged until equilibration is approximated, and in this way expiratory elevation of nitrogen would be minimized. This would, of course, lengthen the time for the procedure. There appears to be a sharp division between normal and emphysematous persons in the number of maximum breathing capacity type of breaths required to produce nitrogen equilibrium. Although quantitation of this impairment is not possible at present, the striking difference suggests a useful screening procedure.

Since diffuse obstructive emphysema is characterized physiologically by a subnormal MBC, elevated residual volume and abnormal lung rinsing (distribution, mixing, and tidal volume to residual volume ratio), the apparatus and methods described might be expected to recognize preclinical stages of the disease In addition, quantitation of the ventilatory impairment can b obtained Direct reading of the MBC and vital capacity, and the use of nomogram for calculating residual volume facilitate the speed of measurement

SUMMARY

1 A direct reading spirometer is described and dynamically evaluated

2 A method for simultaneous measurement of MBC, pulmonary volumina and effective lung ventilation is described and compared to conventiona measurements for the same estimates in normal and emphysematous persons

REFERENCES

1 Comroe, J Methods in Medical Research, Chicago, 1950, Year Book Publishers, vol 2 p 193
2 Comroe, J Methods in Medical Research, Chicago, 1950, Year Book Publishers, vol 2 p 195

(For Discussion, see page 703)

AN ACRYLATE-AMIDE FOAM ARTERIAL PROSTHESIS

Richard W. Hardy, Captain, MC, USAR (by invitation), Carl A. Nielson (by invitation), Roger T. Sherman, Major, MC, USAR (by invitation), Fred Leonard, Ph.D.* (by invitation), and William H. Moncrief, Jr., Lieutenant Colonel, MC, USA (by invitation), Washington, D. C.*

INTRODUCTION

Due to the complex nature of the difficulties involved, it does not seem likely that prevention of degenerative or congenital lesions of the vascular system will be achieved in the near future. It is probable that traumatic lesions will always require surgical management. Therefore, arterial repair and replacement are and will continue to be lifesaving restorative procedures. It is the aim of this investigation to devise a more satisfactory prosthesis to accomplish this replacement. A review was made of previous experiments in arterial replacement.[1-68] The factors involved in the success or failure of these experiments provided insight as to the qualifications of an ideal arterial prosthesis. This review was coupled with a study of the physical characteristics of normal human arteries. From these studies the characteristics of an ideal arterial prosthesis are derived. These are: (1) be nontoxic, noncarcinogenic, nonallergenic, (2) incite little inflammatory or foreign body response, (3) have capacity for intimization with incorporation by fibrous ingrowth, (4) have strength to withstand arterial pressure indefinitely, (5) be initially porous with ability to become rapidly impervious to blood, (6) be elastic and flexible, (7) be easily inserted, (8) have a smooth internal wall, (9) be easily sterilized and stored, and (10) be easily manufactured at a nonprohibitive price. In addition, studies of normal arteries reveal that "the smooth muscle—elastic tissue network responsible for the aortic retractile force over a rather wide range of distension shows mechanical and thermal properties often associated with rubber."[69] To meet this requirement of elasticity, the search for a more ideal prosthetic material was limited to the elastomers. Of this group of materials, Kel-F† elastomer and an acrylate-amide elastomer‡[70] developed at the Army Prosthetics Research Laboratory were

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*Army Prosthetics Research Laboratory, Walter Reed Army Medical Center.

†Manufactured by the Minnesota Mining and Manufacturing Company, St. Paul, Minn.

‡Acrylate-amide elastomer is a polyacrylic ester rubber; a terpolymer of butyl acrylate (90 parts), methyl methacrylate (7.5 parts) and methacrylamide (2.5 parts) with ethyl methacrylate filler (37 parts).

selected because of their quality of inertness Subsequent to their selection, two new elastomers, Hypalon* and Viton,* having potentially similar desirable qualities, have become commercially available

To achieve ease of handling and rapid intimization with minimal initial bleeding after insertion, a foam construction was selected for the prosthesis Considerable difficulty has been encountered in the development of a foam of proper pore size and consistency from these elastomers This has been accomplished to date with the acrylate amide elastomer

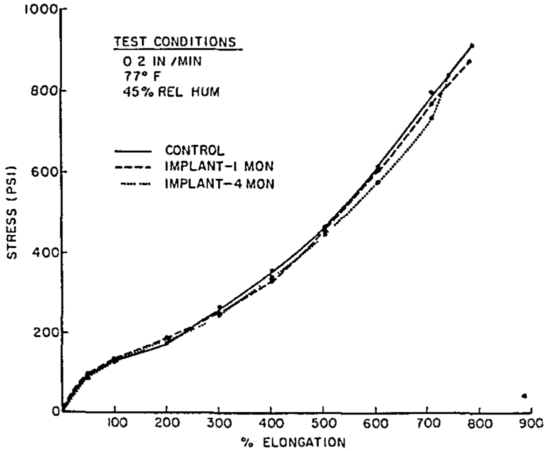

Fig 1 —Stress strain curves for acrylate amide films implanted subcutaneously in dogs for 1 and 4 months Instron testing machine

EVALUATION OF PHYSICAL PROPERTIES

The inertness of acrylate amide elastomer was evaluated by analysis of stress strain deviation after implantation and by tissue reaction Die cut strips of cast acrylate amide film were implanted in the subcutaneous tissue of dogs These strips were removed at intervals of 1 and 4 months after implantation, and were tested by stress strain analysis against control samples The results of this test are graphically illustrated in Fig 1 No measurable degradation appears to have occurred in the acrylate amide elastomer during the time of implantation Long term studies are being made to determine whether degradation will occur on extended exposure to body fluids

Similar die cut strips of acrylate amide film and foam were inserted subcutaneously in dogs and removed at 1, 4, and 5 month intervals to evaluate tissue reaction The elastomer was grossly well tolerated without extrusion or fluid collection Microscopic study of the tissue adjacent to the implanted

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*Manufactured by E I Dupont de Nemours & Co Inc New York N Y

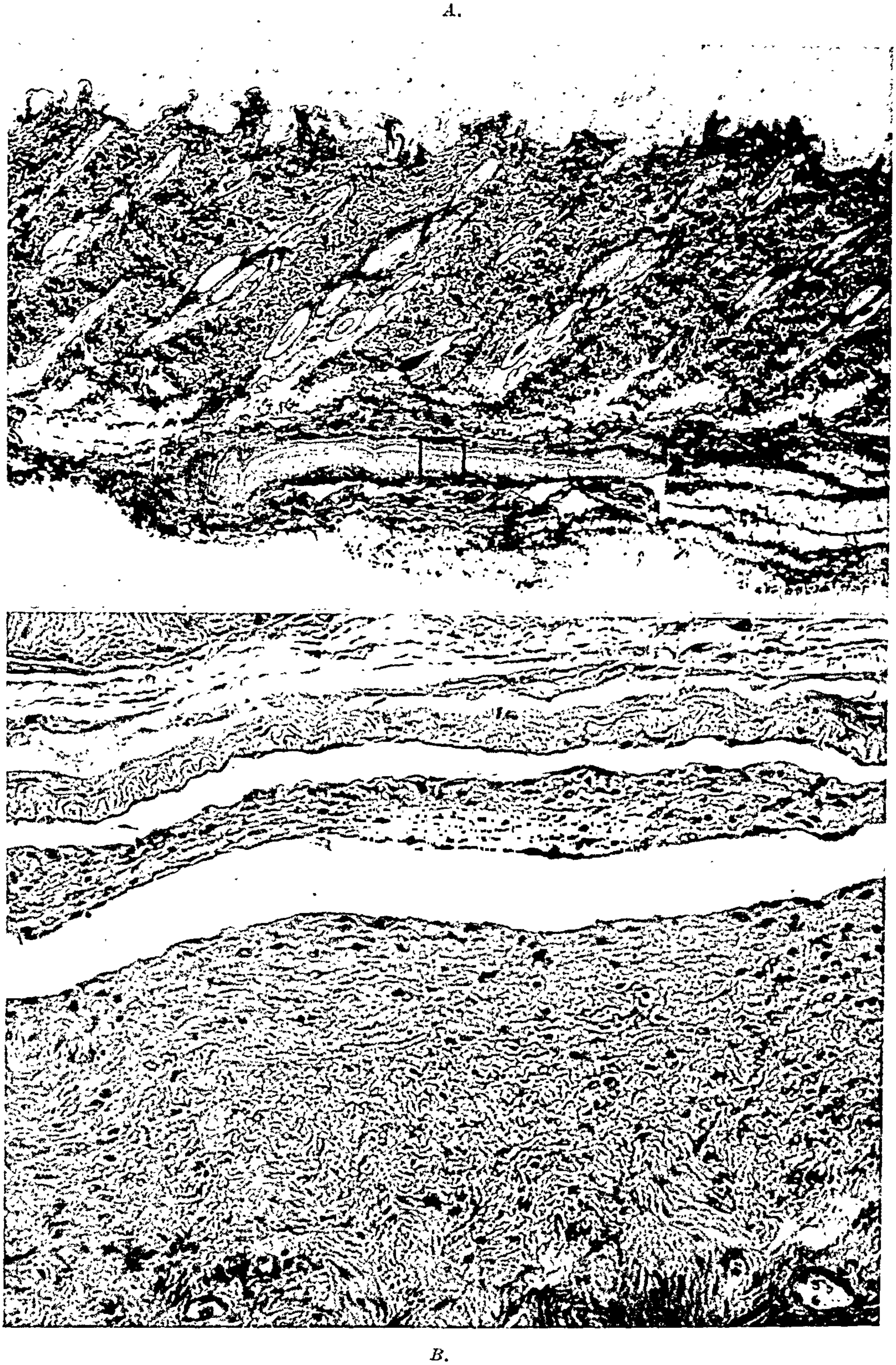

Fig. 2.—*A*, Site of implantation of acrylate-amide film in subcutaneous tissue, 4 months' duration. The film has been removed. Blocked area is shown in higher magnification. (Rinehart ×16; reduced ½.)

B, *Marginal cellular reaction consists mainly of fibroblasts. Occasional lymphocytes are apparent and, in the deeper parts, endothelial elements. Note absence of necrosis, foreign body type giant cells, and polymorphonuclear leukocytes.* (Hematoxylin and eosin ×234; reduced ½.)

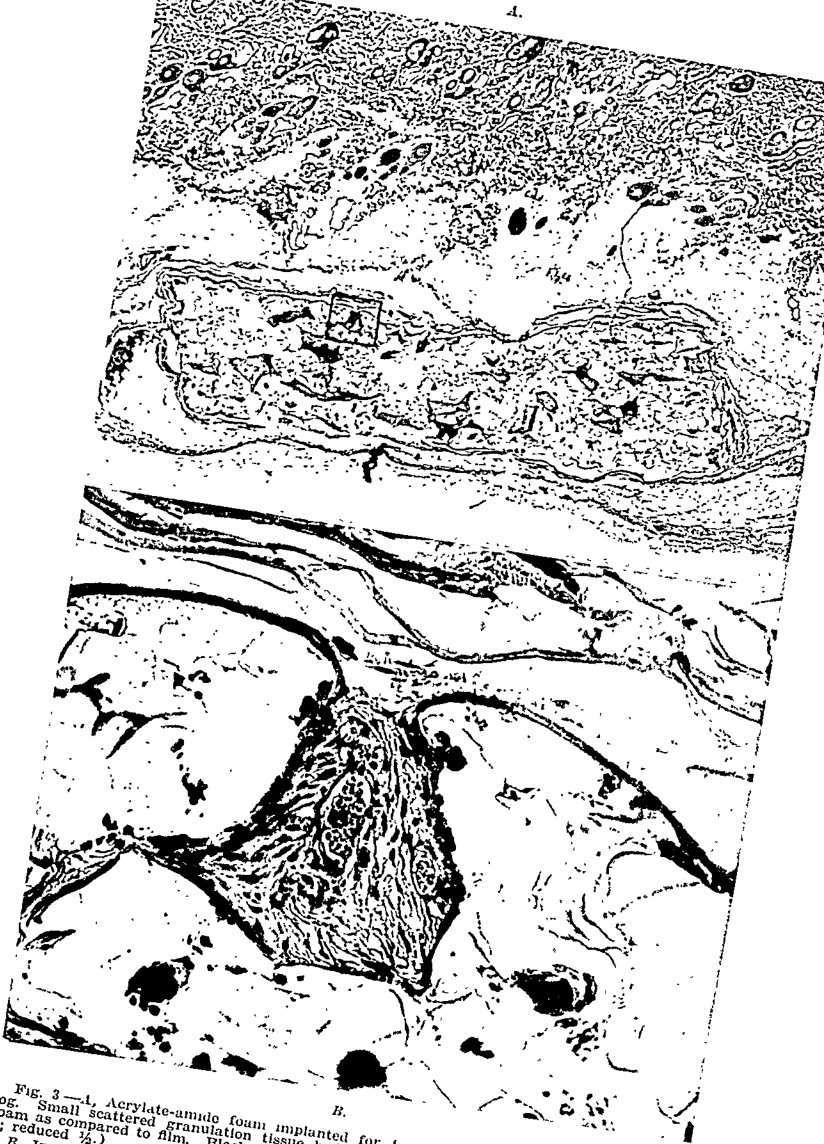

Fig. 3.—A, Acrylate-amide foam implanted for 4 months in the subcutaneous tissue of a dog. Small scattered granulation tissue buds are visible. Note scanty marginal reaction to foam as compared to film. Blocked area is shown in higher magnification in B. (Rinehart ×16; reduced ½.)

B, Ingrowth of connective tissue into acrylate-amide foam. Granulation tissue bud is omposed of fibroblasts and endothelial elements with occasional formed capillaries. Some istiocytes and occasional lymphocytes are apparent also. (Hematoxylin and eosin ×234; educed ½.)

material revealed connective tissue proliferation about the film (Fig. 2) and into the foam (Fig. 3). The cellular reaction to the material was very slight and consisted of occasional lymphocytes, histiocytes, and rare polymorphonuclear leukocytes. No multinucleated giant cells were found and there was no evidence of necrosis; findings which one might expect with chemical irritation or inflammation.

The fabrication of the foamed elastomer into tubular forms and flat sheets was made by forming foamed acrylate-amide elastomer over a glass mandril.

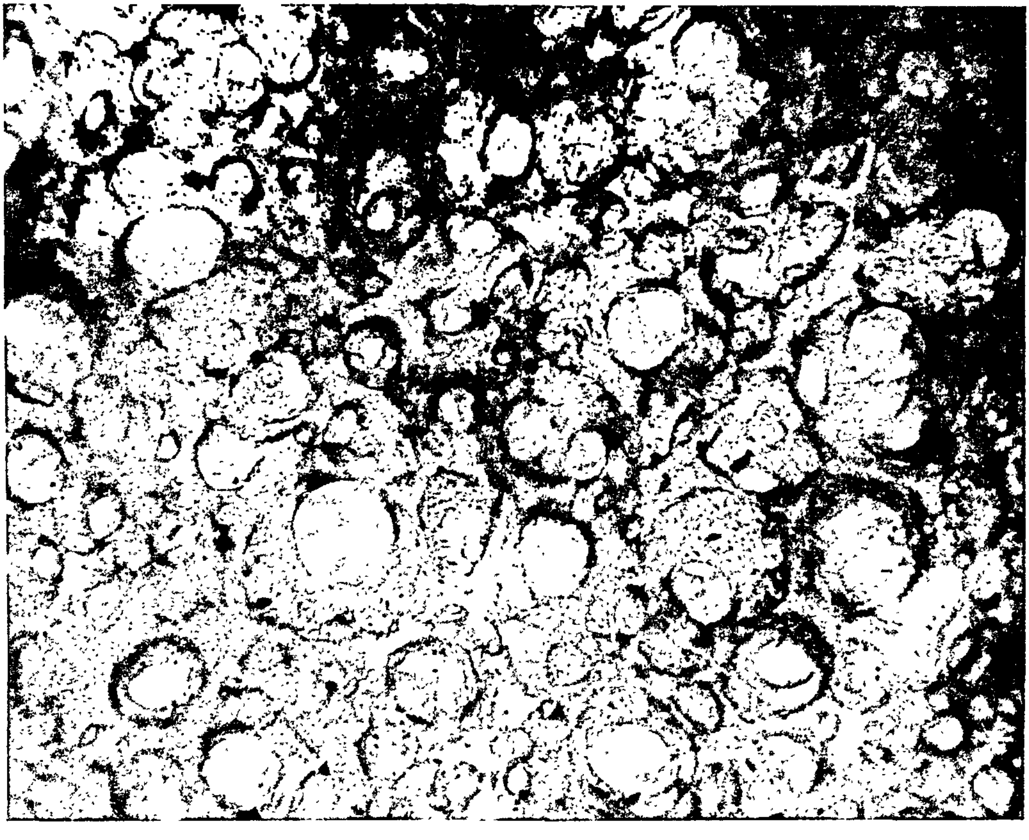

Fig. 4.—Photomicrograph of acrylate-amide foam showing open-cell structure. (×32; reduced ½.)

Optimal pore size was determined by a pilot experiment using Ivalon prostheses of varying known pore sizes and, finally, by trial and error with the acrylate-amide elastomer. Pore size of our present prosthesis varies from 30 to 600 μ with a mean of approximately 250 μ and may be altered to meet varying intravascular pressures (Fig. 4).

Because the tensile strength of a foam is inherently variable, rupture occurred in some of the early model prostheses. Therefore, the prostheses were reinforced with a porous woven tube of two-way stretch Dacron fabric by bonding the tube to the inside of the graft in the foaming process. This has not altered the elasticity of the foam prosthesis. Tensile strength of the woven Dacron reinforcement is 42 pounds per linear inch of cloth.

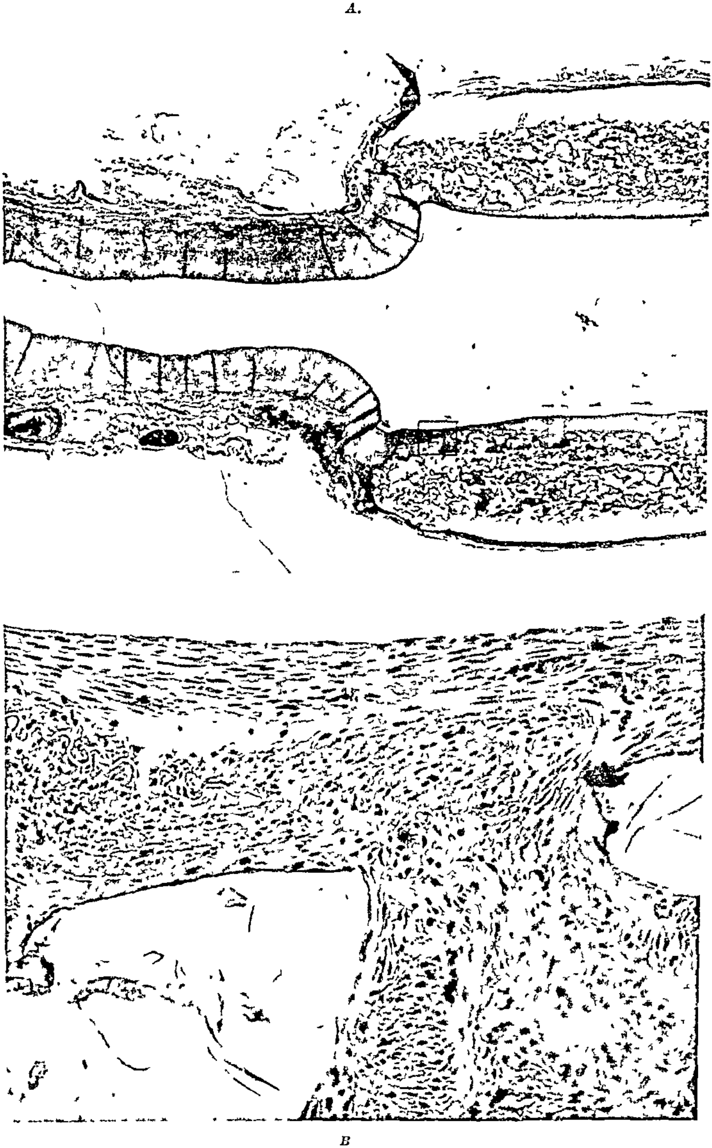

Fig 5 —*A*, Longitudinal section of unreinforced acrylate amide abdominal aortic graft removed from dog at 8 weeks Blocked area is shown in higher magnification in *B* (Hematoxylin and eosin ×71, reduced ½)

B, The internal elastic layer of the aorta is visible in the left half of the figure, and the overlying intima shows slight to moderate thickening The intima of the aorta merges imperceptibly with the intima of the graft (Hematoxylin and eosin ×234, reduced ½.)

EXPERIMENTAL LABORATORY APPLICATION

Twenty-two segments of abdominal aorta and seven superficial femoral arteries of dogs have been replaced by acrylate-amide foam prostheses. The internal diameter of the aortas varied from 5 to 8 mm. while that of the femoral artery segments varied from 2.5 to 4.5 mm. Four dogs have been sacrificed, 1 at 4 weeks, 2 at 8 weeks, and 1 at 12 weeks. All arteries removed at sacrifice were patent. A follow-up on the remaining twenty-four prostheses is being carried out for the effects of long-term use. To date, all are patent. Intimization of our present prosthesis is complete by 8 weeks and has a mean thickness of approximately 280 μ (Fig. 5). The rate of intimization varies with porosity and was not complete by 12 weeks in an early model prosthesis of small pore size. Bleeding through the pores of the prosthesis is moderate and terminates in 5 to 20 seconds without preclotting. The average estimated blood loss through the interstices of an abdominal aortic prosthesis of 3 to 4 cm. in length is 10 c.c.

Acrylate-amide foam sheets reinforced with Dacron fabric have been implanted in the pulmonary outflow tract of 4 dogs. A segment of right ventricle and pulmonary artery was grasped in a partial occluding clamp and an elliptical defect was created in the wall of the right ventricular outflow tract, extending across the annulus of the pulmonary valve. The graft was inserted in the defect and sutured with a running, over-and-over stitch of 5-0 polyethylene monofilament suture.* Blood loss through the graft was minimal. One of the dogs was heparinized with 1.0 mg. heparin per kilogram at the time of insertion of the prosthesis. The prosthesis was not preclotted. Upon release of the clamps, bleeding through the prosthesis was minimal and stopped after 1½ minutes of digital pressure. Estimated blood loss was 15 c.c. All dogs tolerated the procedure without complication. One dog was sacrificed at 1 month to ascertain degree of intimization, which was found to be complete. The remaining 3 dogs will be kept for long-term study.

DISCUSSION

A new arterial prosthesis has been fabricated, possessing characteristics which approach our criteria for the ideal arterial prosthesis. It is made of a new terpolymer, an acrylate-amide elastomer, which has been shown to incite little inflammatory or foreign body response. It is nontoxic and, in the foam state, capable of being incorporated in the body tissues by ingrowth of fibrous tissues. The outstanding characteristics of the acrylate-amide prosthesis are its ease of handling, suturing, and insertion. The resiliency of the foam is such that anastomosis is accomplished with little if any bleeding at this site. The graft can be cut at any angle without fraying. Because of its foam construction, bleeding through the interstices is slight, although pore size is sufficiently large to permit early ingrowth of fibrous tissue and rapid intimization.

The prosthesis can be fabricated with varying degrees of elasticity and its flexibility is maintained after implantation. It has a smooth internal wall and has been used successfully to replace vessels having an internal diameter as small as 2 5 mm Repeated autoclaving causes no degradation of the plastic nor loss of tensile strength

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*Linear monofilament polyethylene suture. For investigational use by Davis and Geck, Surgical Products Division of the American Cyanamide Co., New York, N. Y.

Manufacture at this time is on a laboratory scale but techniques of fabrication are being improved As yet, complex shapes (bifurcations and arches) have not been produced

SUMMARY

An arterial prosthesis has been developed utilizing a Dacron fiber reinforced foam of a new acrylate amide elastomer Laboratory application leads to the impression that this prosthesis will make feasible more successful replacement of arteries of small diameter

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